WORLD HEALTH ORGANIZATION
GLOBAL PROGRAMME TO ELIMINATE
LYMPHATIC FILARIASIS

MONITORING AND
EPIDEMIOLOGICAL ASSESSMENT
OF MASS DRUG ADMINISTRATION

LYMPHATIC FILARIASIS

TAS

A MANUAL FOR NATIONAL ELIMINATION PROGRAMMES

World Health Organization

WORLD HEALTH ORGANIZATION
GLOBAL PROGRAMME TO ELIMINATE
LYMPHATIC FILARIASIS

MONITORING AND
EPIDEMIOLOGICAL ASSESSMENT
OF MASS DRUG ADMINISTRATION

LYMPHATIC FILARIASIS

TAS

A MANUAL FOR NATIONAL ELIMINATION PROGRAMMES

World Health Organization

WHO Library Cataloguing-in-Publication Data

Monitoring and epidemiological assessment of mass drug administration in the global programme to eliminate lymphatic filariasis: a manual for national elimination programmes.

1.Elephantiasis, Filarial - drug therapy. 2.Elephantiasis, Filarial - epidemiology. 3.Pharmaceutical preparations - supply and distribution. 4.Filaricides -administration and dosage.5.National health programs. 6.Manuals. I.World Health Organization.

ISBN 978 92 4 150148 4 (NLM classification: WC 880)

© World Health Organization 2011

All rights reserved. Publications of the World Health Organization are available on the WHO web site (www.who.int) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int).

Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press through the WHO web site (http://www.who.int/about/licensing/copyright_form/en/index.html).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Printed in France.

WHO/HTM/NTD/PCT/2011.4

'This document was printed with the generous support of the Government of Japan.

Contents

Preface v
Acknowledgements vi
Abbreviations ix
Glossary xi
Overview of changes between the 2005 and 2011 editions xvii

1. Eliminating lymphatic filariasis **1**
1.1 Background 1
1.2 Integrating elimination within a framework of neglected tropical disease control 2

2. Recommended strategy for interrupting transmission **5**
2.1 Programmatic steps 5
2.2 Importance of monitoring and evaluation 6

3. Diagnostic tools **7**
3.1 Blood films 7
3.2 Immunochromatographic tests 7
3.3 Brugia Rapid™ 8
3.4 Polymerase chain reaction 8

4. Mapping **9**
4.1 What geographical level should be used for mapping? 9
4.2 How should mapping be implemented? 10

5. Monitoring coverage of mass drug administration **12**
5.1 What geographical area should be used for monitoring? 12
5.2 Which monitoring indicators are needed? 13

6. Assessing the impact of mass drug administration through sentinel and spot-check sites **18**
6.1 What geographical area should be used to assess impact? 18
6.2 When should assessment occur? 20
6.3 How should assessment be implemented? 21
6.4 How does this approach relate to an integrated strategy for control of neglected tropical diseases? 21

7. Transmission Assessment Surveys **22**
7.1 What geographical areas should be used? 22
7.2 When should surveys occur? 23
7.3 How should surveys be implemented? 23

8. Implementing activities and surveillance after mass drug administration has stopped **30**
8.1 What other activities will be implemented after mass drug administration has stopped? 30
8.2 What type of surveillance should be implemented? 31
8.3 What other potential surveillance strategies are available? 33

9. Verifying the absence of transmission **34**
9.1 Background 34
9.2 The dossier 35
9.3 Proposed verification process 37

10. References and other sources of information **39**
10.1 References 39
10.2 Other sources of information 42

Annexes **43**
Annex 1: Measuring the prevalence and density of microfilaraemia in sentinel and spot-check sites 43
Annex 2: Immunochromatographic test protocol 51
Annex 3: Brugia Rapid™ test protocol 53
Annex 4: Cluster-survey protocol for assessing coverage of mass drug administration 56
Annex 5: Detailed protocol for Transmission Assessment Survey 71

Preface

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched by the World Health Organization (WHO) in 2000. Since then, coverage of mass drug administration (MDA) using combinations of two medicines recommended by WHO has expanded from 3 million people in 12 countries in 2000 to more than 496 million people in 53 countries in 2009.

The Programme includes two main components:

- interrupting transmission of lymphatic filariasis (LF); and
- managing morbidity and preventing disability.

In 2010, WHO published GPELF's progress report and strategic plan to review the first 10 years of the Programme and outline an approach and milestones for the second 10 years.[1] One of the milestones in the Strategic Plan is to publish revised guidance for monitoring and evaluation of national LF elimination programmes.

This document focuses only on updating procedures for monitoring and evaluation in line with the programme's first component: to interrupt transmission of LF through MDA. Guidance on activities for the second component is being developed separately.

What is the aim of this manual?

Effective monitoring, epidemiological assessment and evaluation are necessary to achieve the aim of interrupting LF transmission. This manual is designed to ensure that national elimination programmes have available the best information on methodologies and procedures for (i) monitoring MDA, (ii) appropriately assessing when infection has been reduced to levels where transmission

[1] *Global Programme to Eliminate Lymphatic Filariasis progress report 2000–2009 and strategic plan 2010–2020.* (WHO/HTM/NTD/PCT/2010.6). Geneva, World Health Organization, 2010.

is likely no longer sustainable, (iii) implementing adequate surveillance after MDA has ceased to determine whether recrudescence has occurred, and (iv) preparing for verification of the absence of transmission. The manual provides general guidance to national programmes; relevant background information on technical issues is contained in the annexes. As real-life situations may not correspond to predefined categories, consultation with WHO and experts is recommended in complicated situations.

The first edition of this document was published in 2005.[2] In 2010, the STAG-NTD recommended that WHO revise the 2005 document to provide clearer and more feasible methodologies to national programmes on monitoring, epidemiological assessment and evaluation in order to achieve the global target of eliminating LF by 2020. This revised document reflects better understanding of epidemiological aspects of the disease, further field experience, and operational research in monitoring and evaluation of activities to eliminate LF.

For whom is this manual intended?

This manual is intended for managers of national LF elimination programmes; programme staff working at national, regional and district levels; development and technical agencies; nongovernmental organizations; regional programme review groups (RPRGs); and other organizations involved in supporting MDA activities for LF.

[2] *Monitoring and epidemiological assessment of the programme to eliminate lymphatic filariasis at implementation unit level.* (WHO/CDS/CPE/CEE/2005.50). Geneva, World Health Organization, 2005.

Acknowledgements

The World Health Organization (WHO) acknowledges all those who have contributed to the development of materials from which this manual on monitoring and epidemiological assessment of mass drug administration for lymphatic filariasis (LF MDA) has emerged.

The first draft of this document benefited from valuable input from the STAG-NTD Monitoring and Evaluation Sub-Working Group on Disease-Specific Indicators. A WHO Informal Consultation on monitoring and evaluation for LF MDA was held in Geneva, Switzerland, on 16–17 September 2010. This group reviewed the draft document and guided the revision process both at the meeting and during subsequent e-mail consultation based on the comments recieved. Ms Molly Brady and Dr Kazuyo Ichimori, WHO Department of Control of Neglected Tropical Diseases prepared the final draft.

Abbreviations

Ab	antibody
Ag	antigenaemia
DEC	diethylcarbamazine (citrate)
EA	enumeration area
ELISA	enzyme-linked immunosorbent assay
EU	evaluation unit
ICT	immunochromatographic test
IU	implementation unit
LF	lymphatic filariasis
LQAS	lot quality assurance sampling
MDA	mass drug administration
Mf	microfilaraemia
NTD	neglected tropical disease
PCR	polymerase chain reaction
RPRG	regional programme review group
STAG-NTD	Strategic and Technical Advisory Group on Neglected Tropical Diseases
STH	soil-transmitted helminthiases
TAS	transmission assessment survey
WHO	World Health Organization

Glossary

The definitions given below apply to the terms as used in this manual. They may have different meanings in other contexts.

absence of LF transmission
Reduction in transmission of the parasite to a level where continued transmission and recrudescence are not expected.

antibody
A protein produced by the human immune system in response to a foreign substance (antigen) to fight off infection. An antibody reacts specifically with the antigen that triggered its formation and its function is to facilitate removal of the antigen from the body.

antigen
Any foreign substance that stimulates the human immune system to produce antibodies.

antigenaemia
Presence of an antigen circulating in the bloodstream.

at-risk population
Total population in the endemic implementation unit(s).

Brugia malayi area, *Brugia timori* area, *Wuchereria bancrofti* area
Geographical areas with established transmission of the parasite.

clinical case
An individual with any of the clinical findings of hydrocoele, chylocoele, lymphoedema, chyluria, haematochyluria, haematuria, hyper-eosinophilia or tropical pulmonary eosinophilia syndrome; for which other causes have been excluded in a resident of, or long-term visitor to, an endemic area, plus specific antibody elevations in visitors to endemic regions.

critical cut-off threshold
The threshold of infection prevalence below which transmission is likely no longer sustainable, even in the absence of control interventions. The transmission assessment survey estimates this threshold by the number of antigen-positive or antibody-positive cases.

drug coverage
Proportion of individuals, expressed as a percentage, in a targeted population who swallowed a drug, or a combination of drugs.

endemic area
Implementation unit where the average resident population, or any subunit of population, has an antigenaemia or microfilaraemia positivity rate equal to or greater than 1%.

enumeration area
The smallest area for which census population results are available.

epidemiological drug coverage (programme coverage)
Proportion of individuals in the implementation unit who have ingested the MDA drugs of the total population in the implementation unit.

evaluation unit (EU)
A study area selected for implementation of the transmission assessment survey, which can comprise multiple implementation units, or part of an implementation unit.

first- and second-year primary-school children
Children enrolled in either the first or second year of primary education.

geographical coverage
Proportion of administrative units that are implementing MDA of all those that require MDA.

implementation unit (IU)
The administrative unit in a country which is used as the basis for making decisions about implementing MDA. The IU must be defined before mapping takes place.

ineligible population
Group of individuals not qualified or entitled to receive anthelminthic treatment in preventive chemotherapy interventions. Ineligibility is usually determined by exclusion criteria based on drug safety.

KAP survey
An assessment of the knowledge, attitudes and practices of a community or group of individuals at one point in time, usually with respect to a health or health-related topic.

lymphatic filariasis
A parasitic infection of humans caused by nematodes (worms) of the Filariodidea family. *Wuchereria bancrofti* cause the majority (90%) of human infections, which are mostly acquired in childhood; *Brugia malayi* and *Brugia timori* cause the

remainder. *Anopheles*, *Aedes* and *Culex* mosquitoes are the main vectors responsible for transmission. Mosquitoes serve as biological hosts that both develop and transmit the parasite during blood-feeding and establish the infection in humans.

lymphatic filariasis case

While clinicians will use "lymphatic filariasis case" to mean a person with clinical disease, in this manual we use it to mean an individual having current infection with *Brugia malayi*, *Brugia timori* or *Wuchereria bancrofti*, whether or not microfilaraemic.

lymphatic system

The delicate network of nodes and vessels that maintain the delicate balance between the tissues and blood in humans. The lymphatic system is an essential component of the body's immune defence system.

mass drug administration (MDA)

A modality of preventive chemotherapy in which anthelminthic medicines are administered to the entire population of an area (e.g. state, region, province, district, sub-district, village) at regular intervals, irrespective of the individual infection status.

mapping

An estimate of prevalence of microfilaraemia or antigenaemia in at least one high-risk area in an implementation unit. It is used to determine if a high enough level of infection is present to sustain transmission and if the implementation unit should be classified as endemic.

MDA round

Distribution of antifilarial medicines to the target population during a defined time period. Normally, MDA activities cannot be conducted simultaneously throughout a country, so a "round" may take one or two weeks or more before being completed at a national level.

microfilariae

Microscopic larval stage of LF parasites that circulates in the blood and is transmitted by mosquitoes.

microfilaraemia

Presence of microfilariae in the blood.

morbidity

Clinical consequences of infections and diseases that adversely affect the health of individuals. Lymphatic filariasis causes chronic morbidity through damage to the lymphatic system, kidneys, arms, legs or genitals (especially in men).

neglected tropical diseases (NTDs)

A group of primarily infectious diseases which thrive in impoverished settings, especially in the heat and humidity of tropical climates. They have been largely eliminated elsewhere and thus are often forgotten. WHO focuses on control of 17 NTDs: dengue, rabies, trachoma, Buruli ulcer, endemic treponematoses, leprosy,

Chagas disease, human African trypanosomiasis, leishmaniasis, cysticercosis, dracunculiasis, echinococcosis, foodborne-trematode infections, lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiases.

net primary-school enrolment ratio
The number of children enrolled in primary school that belong to the age group that officially corresponds to primary schooling, divided by the total population of the same age group.

national coverage
Proportion of individuals in an endemic country requiring MDA for LF who have ingested the appropriate drugs.

preschool-aged children
All children between the ages of 1 and 5 years who are not yet attending (primary) school.

prevalence of infection
The proportion, expressed as a percentage, of individuals infected with a parasite species.

preventive chemotherapy
The use of anthelminthic drugs, either alone or in combination, as a public health tool against helminth infections. MDA is one modality of preventive chemotherapy.

recrudescence
A new outbreak of infection after a period when transmission is controlled.

reported coverage
Intervention coverage calculated from data reported by all drug distributors.

school-aged children
All children between the ages of 6 and 15 years (usually), regardless of whether they are attending school. In some countries, enrolment may include individuals older than 15 years.

sentinel site
A geographical area, with a population of at least 500 people, selected in order to collect parasitological data to monitor the success of the programme. It should remain the same throughout the course of the programme.

spot-check site
A geographical area, with a population of at least 500 people, selected in order to collect parasitological data to complement data collected in sentinel sites. Spot-check sites should be chosen for each assessment and will change over the course of the programme.

soil-transmitted helminthiases (STH)
Parasite infections attributed to four species of nematodes: roundworms (*Ascaris lumbricoides*); whipworms (*Trichuris trichiura*) and hookworms (*Necator americanus* and *Ancylostoma duodenale*).

surveillance
The ongoing, systematic collection and evaluation of data describing the occurrence and spread of disease. The part of the programme aimed at the discovery, investigation and elimination of continuing transmission, the prevention and cure of infections, and the final substantiation of claimed absence of transmission.

surveyed coverage
A method used to verify reported coverage through use of population-based cluster survey methods. It is calculated as the total number of individuals identified by household survey as having ingested the drugs of the total number of individuals residing in all the surveyed households about whom information on drug ingestion could be elicited.

target population (LF target population = eligible population)
The population in an implementation unit that is targeted for treatment. For LF, the target population is the same as the eligible population, that is, those individuals who are eligible to receive the drugs, based on the criteria for drug safety, and is usually 85–90% of the total population.

transmission assessment survey (TAS)
A survey designed to measure whether evaluation units have lowered the prevalence of infection to a level where recrudescence is unlikely to occur, even in the absence of MDA interventions.

verification
The procedure for countries to present evidence for external verification of absence of LF transmission and receive official recognition for the success of their efforts.

Overview of changes between the 2005 and 2011 editions

The table below outlines the major technical revisions to the 2005 edition of this document.

Overview of changes between the 2005 and 2011 editions

Technical issue	2005	2011
Number of sentinel and spot-check sites	Two sites each per IU containing populations of at least 500 people each	At least one site each per IU containing populations of at least 500 people each (in order to collect at least 300 samples each)
Data collection times in sentinel and spot-check sites	Baseline Before third MDA Before fifth MDA	Baseline Before fourth MDA (optional) Before sixth MDA (a sixth MDA will likely be conducted in any case)
Measurement of clinical manifestations	Included in section on sentinel sites	Deleted
Geographical area for Transmission Assessment Survey (TAS)	Implementation unit (IU)	Evaluation unit (EU)

Technical issue	2005	2011
Other criteria for implementing TAS	Prevalence of Mf is <1% in sentinel and spot-check sites before fifth MDA In areas where *Wuchereria Bancrofti* is endemic, no children aged 2–4 years test Ag-positive in sentinel and spot-check sites Prevalence of Mf is <1% and no 2–4-year olds test Ag-positive in 5–10 additional spot-check sites No Ag-positives in community-based LQAS cluster survey of 300 children aged 2–4 years in high-risk areas	Prevalence of Mf is <1% in sentinel and spot-check sites after fifth MDA, with at least 65% coverage of total population in each MDA
TAS design	LQAS survey of 3000 school entrants in IU	If the net primary-school enrolment ratio is ≥75%, cluster survey or systematic sampling with LQAS analysis in schools If the net primary-school enrolment ratio is <75%, cluster survey or systematic sampling with LQAS analysis in the community
TAS target group	School entrants (assumed to be children aged 6 years)	If school-based survey, children in first and second years of primary school If community-based survey, children aged 6–7 years
TAS diagnostic tools	ICT NOW USING FILARIASIS TEST STRIP (FTS)	ICT in areas where *W. bancrofti* is endemic Brugia Rapid™ in areas where *Brugia spp*. is endemic
TAS cut-off criteria	Zero Ag-positives	In areas where *W. bancrofti* is endemic, Ag <2% where *Anopheles* and/or *Culex* are the principal vectors[1] In areas where *W. bancrofti* is endemic, Ag <1% where *Aedes* is the principal vector[2] In areas where *Brugia spp*. is endemic, Ab <2% In areas where *W. bancrofti* and *Brugia spp*. are co-endemic, evaluate Ag and Ab results separately against cut-off points
Post-MDA surveillance	Ag testing in sample of 3000 children aged 5 years carried out 5 years after stopping MDA	TAS, carried out at approximately 2–3 years and 5–6 years after original survey Ongoing surveillance begun as early as possible

Ab =antibody; Ag = antigenaemia; EU = evaluation unit; ICT = immunochromatographic test; IU = implementation unit; LQAS = lot quality assurance sampling; MDA = mass drug administration: Mf = microfilaraemia; TAS = transmission assessment survey.

[1] The reason is that in endemic areas for *W. bancrofti*, Ag prevalence is always higher than Mf prevalence; therefore the <2% prevalence target for Ag is used as a conservative proxy for an Mf prevalence of <1%.

[2] The reason is that in endemic areas for *W. bancrofti*, Ag prevalence is always higher than Mf prevalence; therefore the <1% prevalence target for Ag is used as a conservative proxy for an Mf prevalence of <0.5%.

1 Eliminating lymphatic filariasis

1.1 Background

Before the launch of the Global Programme to Eliminate Lymphatic Filariasis (GPELF) by the World Health Organization (WHO) in 2000, lymphatic filariasis (LF) was endemic in more than 80 countries and territories and the number of people at risk of infection exceeded 1 billion (*1*). In 1996, WHO estimated that some 120 million people worldwide are affected by LF, of whom about 40 million are incapacitated and disfigured by the disease (*1*). Although not fatal, WHO has ranked LF as one of the world's leading causes of permanent and long-term disability (*2*).

In 1997, the 50th World Health Assembly resolved to eliminate LF as a public-health problem (resolution WHA50.29). In response, WHO proposed a comprehensive strategy for achieving the elimination goal that included interrupting transmission in endemic communities and implementing interventions to prevent and manage LF-associated disabilities (*3, 4*).

WHO recommends therapy using combinations of two medicines delivered to entire populations at risk through a strategy known as mass drug administration (MDA). Ivermectin and albendazole are administered in areas where onchocerciasis is co-endemic; diethylcarbamazine (DEC) and albendazole are administered in areas where onchocerciasis is not co-endemic. These medicines safely and effectively reduce the number of circulating microfilariae in the blood and prevent further transmission from occurring (*5–7*). Ivermectin and albendazole have been donated since the beginning of GPELF; the DEC donation is due to begin in 2012. Annual MDA carried out at adequate levels of coverage – estimated to be at least 65% of the total population in endemic areas – should ultimately make elimination possible (*8–10*).

GPELF began its first MDA campaigns in Egypt and Samoa. By 2009, MDA had covered approximately 496 million people at risk in 53 endemic countries (*11*). Furthermore, 37 countries were in the process of completing their fifth MDA in at least some implementation units and were ready to determine whether to stop MDA and transition to post-MDA surveillance.

1.2 Integrating elimination within a framework of neglected tropical disease control

Since 2000, the context of national LF elimination programmes has changed dramatically. With the move towards integrated preventive chemotherapy programmes to control neglected tropical diseases (NTDs), many national LF elimination programmes are now being co-implemented with programmes to eliminate or control onchocerciasis, schistosomiasis, soil-transmitted helminthiases (STH) and trachoma. In 2006, WHO published *Preventive chemotherapy in human helminthiasis* to assist countries in designing and implementing an integrated approach to the control of these diseases (*12*).

As part of the preventive chemotherapy strategy, many countries are co-implementing distribution of anthelminthic medicines for multiple diseases and including integrated training, supervision and drug delivery. As such, national strategies to control or eliminate NTDs need to consider the changes that will occur after LF MDA has stopped. An important collateral benefit of LF MDA is that of de-worming associated with community-wide distribution of albendazole and ivermectin; these medicines are also highly effective against STH (*13, 14*). As activities carried out by national elimination programmes reduce levels of filarial infection and reach the stopping point for LF MDA, administration of de-worming treatments to populations in need should continue, especially in preschool-aged and school-aged children. The WHO manual on *Deworming school-aged children* provides guidance on how to determine deworming strategies after LF MDA has ceased (*15*).

The algorithms below show two further examples of outcomes in national integrated NTD programmes when LF MDA has stopped (*12*). The first algorithm shows the strategy of integrated MDA in areas endemic for LF; the second shows the changes that occur when LF MDA is no longer needed.

The only strategy that changes in areas co-endemic for onchocerciasis, but not for schistosomiasis or STH, is the treatment regimen. After LF has been eliminated, the strategy changes from annual MDA with ivermectin and albendazole to annual MDA with ivermectin only.

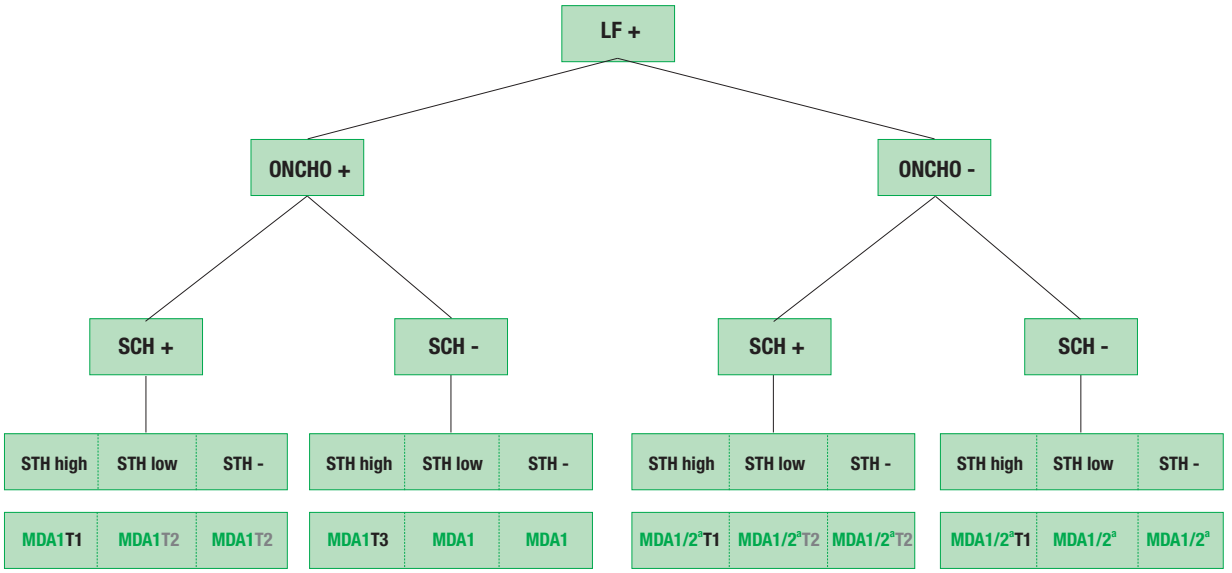
In areas where onchocerciasis is not co-endemic, the approach to MDA will vary depending on the other diseases endemic to the area.

- In areas where LF and schistosomiasis are endemic and STH is highly prevalent, MDA changes from two annual distributions (one with albendazole and DEC and one 6 months later with albendazole and praziquantel) to two annual distributions (one with albendazole and praziquantel and one 6 months later with albendazole only) after LF has been eliminated.

- In areas where LF and schistosomiasis are endemic and STH has a low prevalence, MDA changes from one distribution with albendazole and DEC and a second distribution anytime with praziquantel to only one annual MDA with albendazole and praziquantel.
- In areas where LF and schistosomiasis are endemic, MDA changes from one annual distribution with albendazole and DEC and a second distribution anytime with praziquantel to only one annual MDA with praziquantel.
- In areas where LF is endemic and STH is highly prevalent, MDA changes from two annual distributions (one with albendazole and DEC and one 6 months later with albendazole only) to two annual distributions with albendazole only.
- In areas where LF is endemic and STH has a low prevalence, MDA changes from one annual distribution of albendazole and DEC to one annual distribution with albendazole only.

Furthermore, while the specifics of integration will vary depending on the epidemiological situation of a given country, programme managers should actively pursue potential opportunities to coordinate monitoring, epidemiological assessment and evaluation activities among stand-alone NTD control programmes.

Algorithm 1. Coordinated implementation of preventive chemotherapy interventions



LEGEND:

Mass drug administration

MDA1[a]	IVM+ALB
MDA2[a]	DEC+ALB
MDA3	IVM

Targeted treatment

T1	ALB+PZQ or MBD+PZQ
T2	PZQ
T3	ALB or MBD

Coulour coding

Green: first annual drug distribution

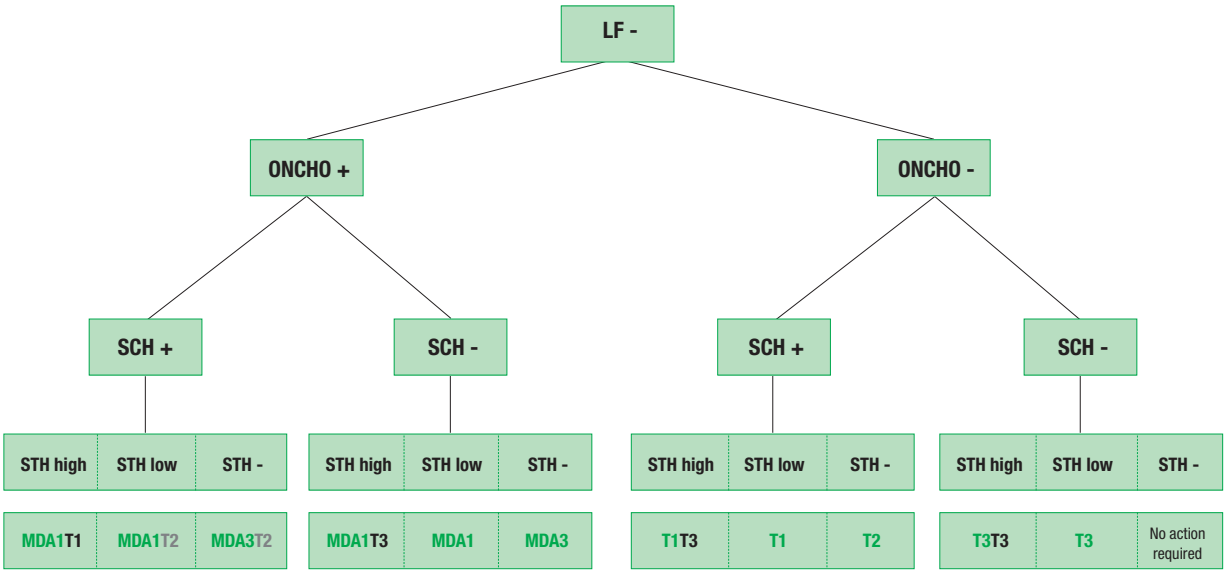
Black: second annual drug distribution, to be carried out 6 months after the first annual drug distribution

Grey: second annual drug distribution, to be carriedout anytime, but at least 1 week after the first annualdrug distribution. In some instances ALB, IVM andPZQ can be coadministred, see Box B, page 14.

[a] MDA1/2: if the country is endemic for ONCHO, IVM (insteadof DEC) should be used to control LF even if ONCHO is nottransmitted in the targeted areas. To control LF, therefore,IVM should be used in ONCHO-endemic countries (MDA1)and DEC in ONCHO-free countries (MDA2), irrespective of whether ONCHO is transmitted in the targeted area.

Source: Preventive chemotherapy in human helminthiasis (12).

Algorithm 2. Coordinated implementation of preventive chemotherapy interventions



LEGEND:

Mass drug administration

MDA1[a]	IVM+ALB
MDA2[a]	DEC+ALB
MDA3	IVM

Targeted treatment

T1	ALB+PZQ or MBD+PZQ
T2	PZQ
T3	ALB or MBD

Coulour coding

Green: first annual drug distribution

Black: second annual drug distribution, to be carried out 6 months after the first annual drug distribution

Grey: second annual drug distribution, to be carriedout anytime, but at least 1 week after the first annualdrug distribution. In some instances ALB, IVM andPZQ can be coadministred, see Box B, page 14.

[a] MDA1/2: MDA1/2: if the country is endemic for ONCHO, IVM (insteadof DEC) should be used to control LF even if ONCHO is nottransmitted in the targeted areas. To control LF, therefore,IVM should be used in ONCHO-endemic countries (MDA1)and DEC in ONCHO-free countries (MDA2), irrespective of whether ONCHO is transmitted in the targeted area.

Source: Preventive chemotherapy in human helminthiasis (12).

2 Recommended strategy for interrupting transmission

In order to interrupt transmission of LF in endemic countries, GPELF recommends the mass administration of effective antifilarial medicines to the entire population at risk for a sufficient period of time. This approach may be supplemented by selective treatment of infected individuals and/or vector control (*3, 4*).

The objective of MDA is to reduce the level of microfilaraemia in infected individuals so that transmission cannot be sustained, even after MDA has been stopped. In this way, transmission is interrupted. The effectiveness of MDA in reducing the prevalence and density of microfilaria in the blood is directly related to the proportion of the population that ingests the medicines every year (*10*). A minimum effective coverage of the total population is considered to be 65% (*9*). However, the number of rounds of MDA will depend on the initial prevalence of infection, the initial intensity of transmission, the efficacy of medicines, the combinations of parasites and vectors, and the density of vectors (*16–20, 10, 21*).

The two principal regimens for MDA are:

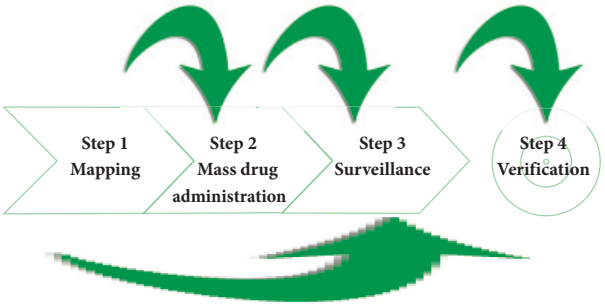
- once yearly treatment with single doses of two medicines administered together: albendazole (400 mg) plus either ivermectin (150–200 mcg/kg) or DEC (6 mg/kg) for 4–6 years (*7*); or
- exclusive use of table salt or cooking salt fortified with DEC for 1–2 years (*22*).

2.1 Programmatic steps

The decision about which type of MDA to implement depends on the local context. This manual focuses on the first regimen, as distribution of DEC-fortified salt currently is used only in a few areas. In either case, the programmatic steps taken to implement and monitor MDA are the same (*Figure 1*).

Step 1 (Mapping) is conducted to determine whether active transmission is occurring and MDA is necessary.

Figure 1. Programmatic steps taken by the Global Programme to Eliminate Lymphatic Filariasis to interrupt transmission[a]



[a]*Source: GPELF Progress report 2000–2009 and strategic plan 2010–2020 (23).*

Step 2 (MDA) includes three approaches to assessing the intervention:

- reported drug coverage after every MDA to monitor implementation, with a coverage survey relying on respondent recall conducted after at least one round of MDA;
- assessment of sentinel and spot-check sites before first MDA, before fourth MDA (optional) and before sixth MDA to determine effectiveness of MDA; and
- transmission assessment survey (TAS) after the sixth MDA[3] to determine if the level of infection has been reduced to a point where it is likely that transmission is no longer sustainable.

Step 3 (Surveillance) is used to monitor infection levels for approximately 5 years after MDA has stopped.

Step 4 (Verification) includes an assessment of detailed historical and epidemiological evidence of the absence of transmission.

National elimination programmes do not end after MDA has been discontinued. Programme staff and resources must be maintained in order to continue surveillance and evaluation activities and manage the morbidity components of the programme. In fact, countries cannot verify elimination of LF directly after MDA has been stopped: approximately 5 years of post-MDA surveillance data are required in order to confirm the sustained absence of transmission.

2.2 Importance of monitoring and evaluation

Effective monitoring and evaluation is important throughout the lifespan of the LF programme. National elimination programmes must be able to effectively monitor MDA, appropriately assess when infection has been reduced to levels where transmission is likely no longer sustainable, and implement adequate surveillance after MDA to reveal whether recrudescence has occurred.

Capacity-building of monitoring and evaluation skills should be a priority for the LF programme from the beginning. While this manual aims to provide guidance to national LF elimination programmes to help them make the best decisions possible, global guidance will not fit every situation. National programmes are encouraged to consult with WHO, RPRGs and experts if specific technical issues arise. In addition, programmes should consider partnerships with local and international academic and research centres to provide technical assistance and independent evaluations of the LF programmes.

[3] Or fifth MDA if sixth was not implemented.

3 Diagnostic tools

The choice of diagnostic tools for monitoring and evaluating national programmes depends upon the sensitivity and specificity of the tools as well as their feasibility in terms of field implementation, technical skills required and cost. A number of diagnostic tools are available to assess the impact of MDA. These include:

- blood films (60-µl thick) to detect the presence of microfilaraemia;
- tests to detect circulating antigen to *Wuchereria bancrofti*, such as the rapid immunochromatographic test (ICT) and laboratory-based antigen enzyme-linked immunosorbent assay (ELISA) Og4C3;
- filarial antibody detection tests for *Brugia spp.*, such as the Brugia Rapid™ test; and
- polymerase chain reaction (PCR) techniques to detect parasite DNA in humans and mosquitoes.

3.1 Blood films

Examining a stained blood slide for microfilaraemia can reveal whether a person has microfilaraemia in the peripheral blood. In areas with nocturnally periodic LF, blood must be taken in the middle of the night. *Annex 1* provides guidance for measuring microfilaraemia prevalence through collection and preparation of blood films.

3.2 Immunochromatographic tests (ICTs)

The rapid ICT antigen detection test is available only for *W. bancrofti*. It measures the presence of adult worm antigen circulating in the blood, and samples

can be taken at any time. People who are treated with antifilarial medicines retain antigen in the blood for several months or years as the adult worms and microfilariae die and disintegrate (*24*). Detection of antigen may therefore still be positive despite a significant reduction in microfilaraemia levels. *Annex 2* includes the protocol for use of ICTs.

3.3 Brugia Rapid™

The Brugia Rapid™ test detects antibodies to *Brugia malayi* and *B. timori* (*25*). Infected people have elevated levels of antibodies, but the results of antibody testing do not distinguish between current and past infection. However, detection in children demonstrates recent infection. *Annex 3* details the protocol for Brugia Rapid™ tests.

3.4 Polymerase chain reaction

Techniques to detect parasite DNA, either in human blood or in mosquito vectors, are not yet routinely used, as they require expensive and complicated laboratory equipment. Molecular xenomonitoring can be used to detect the presence of the parasite in vectors and is a sensitive indicator of microfilaraemia; however, it is not a measure of infectivity or current rates of parasite transmission.

Table 1. Summary of monitoring and evaluation methods in programmatic steps of LF MDA

Step	Indicator	How collected?	Tools	Manual
Mapping	Infection level	Existing information and mapping survey in older school-age or adult populations	*W. bancrofti*: Ag (ICT) or Mf (blood films) *Brugia spp.*: Mf (blood films) Overlap: Ag (ICT) and Mf (blood films)	Pages 9–11
MDA	Drug coverage	Reported and/or surveyed coverage in IU	Register reports or coverage surveys	Pages 12–17
	Infection prevalence	Assessment in sentinel and spot-check sites in IU in population aged >5 years	*W. bancrofti*: Mf (blood films) and/or Ag (ICT) *Brugia spp.*: Mf (blood films)	Pages 18–21
	Infection prevalence	Transmission assessment survey in EU of 6–7-year-olds or first-and second-year primary-school children	*W. bancrofti*: Ag (ICT) *Brugia spp.*: Ab (Brugia Rapid™) Overlap: Ag (ICT) and Ab (Brugia Rapid™)	Pages 22–29
Surveillance	Infection prevalence	Repeat transmission assessment survey in EU; ongoing surveillance	*W. bancrofti*: Ag (ICT) *Brugia spp.*: Ab (Brugia Rapid™) Overlap: Ag (ICT) and Ab (Brugia Rapid™)	Pages 30–33
Verification		Country dossier		Pages 34–37

Ab = antibody; Ag = antigenaemia; EU = evaluation unit; ICT= immunochromatographic test; IU = implementation unit; MDA = mass drug administration; Mf = microfilaraemia

4 Mapping

Mapping, the first programmatic step, is used to assess the disease situation in the country and identify areas where MDA is required by determining where active transmission is occurring. This assessment does not measure the prevalence of microfilaraemia or antigenaemia throughout the IU. Rather, it provides a quick-and-easy estimate of prevalence in at least two areas thought to be at higher risk than other areas for the purpose of assessing whether the prevalence of infection is high enough in these sites to sustain transmission. The result is used to classify the IU as a whole as being endemic or non-endemic.

4.1 What geographical level should be used for mapping?

The mapping process starts by identifying the implementation unit for MDA in the country. The definition of an IU is the administrative unit in a country for which the decision to administer MDA is made, depending on whether indigenous transmission occurs (that is, the status of endemicity) (*3, 4*). The IU must be defined before mapping takes place.

Normally, the choice of which administrative level will constitute the IU is made at national level. In most countries, the second administrative level – usually the district level – is identified as the IU. However, the choice is influenced by feedback received from lower administrative units on the distribution of the disease within those units. If the filarial infection is focal, a lower administrative level may be chosen as the IU, whereas if the infection is more widespread, a higher administrative level may be chosen.

4.2 How should mapping be implemented?

4.2.1 Review of existing information

Identifying areas where MDA might be required involves reviewing a combination of existing information. This includes:

- unpublished and published data on filariasis;
- reports of medical and health services at the district level or its equivalent;
- hospital records on hydrocelectomy; and
- existence and use of local names for the terms "hydrocele" and "lymphoedema".

This review should make it possible to distinguish those areas that require MDA and those that require further investigation.

4.2.2 Implementation of mapping surveys

In areas where *W. bancrofti* is possibly endemic, initial mapping of LF is undertaken using ICT to measure antigenaemia, or, if ICTs are not available, blood films to measure microfilaraemia, in older school-aged or adult populations. Programme managers should recognize that testing for microfilaraemia is not as sensitive as testing for antigenaemia; therefore, countries that use microfilaraemia to identify IUs in need of MDA should consult with WHO and/or the RPRG to decide whether re-mapping using ICTs is necessary in areas with infection levels below the threshold of endemic classification.

In areas where *Brugia spp*. is endemic, initial mapping is implemented using blood films to measure levels of microfilaraemia in older school-aged or adult populations.

If levels of either antigenaemia or microfilaraemia levels are equal to or greater than 1%, the area is designated as needing MDA to eliminate LF transmission (*12*).

Approaches used for mapping differ among regions and countries. For instance:

- In many countries in the Region of the Americas, surveys of antigenaemia levels were implemented among schoolchildren aged 6–10 years.
- In countries of the PacELF subregion, antigenaemia surveys were conducted among different age groups using various sampling approaches.
- In countries of the African Region, antigenaemia surveys of 50–100 people aged >15 years in two villages considered to be most likely for ongoing transmission in each IU were conducted according to recommendations contained in WHO guidelines on rapid mapping (*26*).

4.2.3 Categorization of implementation units

After initial mapping and before IUs are targeted for MDA, the national programme manager should categorize IUs as follows:

- endemic (red): IUs where the average resident population, or any subunit of population (village or urban area), has an antigenaemia (Ag) or microfilaraemia (Mf) positivity rate of 1% or greater;
- non-endemic (green): IUs where either the ecological situation is not conducive to transmission (e.g. generally altitudes above 1600 metres, dry arid areas) or where previous surveys have indicated an Ag or Mf positivity rate of less than 1%;
- uncertain (grey): IUs where the status of LF endemicity is still undetermined and where further surveys are required to assess the infection rate.

5 Monitoring coverage of mass drug administration

Monitoring comprises the routine collection and analysis of data that pertain to the delivery of services. These data are used by managers at all levels to create more effective delivery strategies where gaps in performance have been identified. Monitoring is an essential component of programme management that provides important input into decisions about whether to stop interventions.

Although, in principle, each step of programme implementation can be monitored, MDA coverage is the most practically useful, in particular for monitoring the number of people who have actually ingested the medicines.

5.1 What geographical area should be used for monitoring?

Most decisions on implementation and monitoring are taken at IU level. Programme managers will need to calculate the at-risk, total and target populations in each IU. At the national level, programme managers can also calculate overall statistics, such as national coverage.

5.1.1 Determining the at-risk population in the implementation unit

Once an IU has been defined as endemic for LF (that is, where the prevalence of Ag or Mf is ≥1% in *W. bancrofti* areas and the Mf prevalence is ≥1% in *Brugia spp*. areas), the total population in that IU is considered to be at risk.

5.1.2 Determining the total population in the implementation unit

The following are possible sources of data from which to determine the total population.

- ***Census.*** In many countries a nationwide census is carried out, generally at 10-year intervals, and the data obtained are available from the administrative

units chosen as the IU. To estimate the total population in the years between two censuses it is most common to multiply the base population by the projected population growth rate. For example, if the projected annual growth rate is 3% and the last census was carried out 5 years ago, the projected current population is the population at the time of the last census x 1.035.

- ***Special surveys***. In the absence of census data, surveys might be carried out under the auspices of the ministry of health or other development sectors to estimate the population of the different administrative levels.
- ***Enumeration of the household population before MDA***. In many national elimination programmes, household surveys are carried out to enumerate households to record the target, or eligible, population. These data can also be used for other health activities.

Official census data should be used, if available. However, if the official census is considered inaccurate, the IU should judge which source most accurately reflects its total population. It is advisable to state the source of the data and to use the same source whenever the total population is used for calculating indicators.

5.1.3 Determining the target population in the implementation unit

A certain section of the at-risk population will not be eligible for treatment. They are therefore not included in the population targeted for treatment.

Where co-administration of DEC plus albendazole is used as the MDA regimen, pregnant women, children aged under 2 years and the severely ill should be excluded from MDA (*3*).

Where co-administration of ivermectin plus albendazole is used, pregnant women, lactating women in the first week after birth, children measuring less than 90 cm in height and the severely ill should be excluded from MDA (*4*).

The target, or eligible, population for MDA is the population not excluded according to the above-mentioned criteria. The target population is usually based on official census projections minus 10–15%, depending on estimates of the ineligible population, or calculated by house-to-house registration done directly before the MDA. As far as possible, the same data source for total population and target population should be used.

5.2 Which monitoring indicators are needed?

The objective of MDA is to administer antifilarial medicines, once a year, to all eligible individuals in endemic IUs. The greater the number of people who ingest the medicines, the better the chance of successfully interrupting LF transmission. If programmes conduct MDAs that do not reach critical coverage levels, it is likely that MDA would need to be continued for more years (*27, 28*). Furthermore, if there is evidence of widespread systematic non-compliance, that is, people who never ingest the medicines in any MDA round, this could mean that reservoirs of infection remain in the population and there is an increased chance that LF transmission continues (*16, 16, 29*).

Drug distributors need to be trained and supervised to ensure that they use directly observed treatment whenever possible both to maximize programme impact and to ensure that reported coverage reflects as closely as possible people who actually ingested the medicines (*7, 30, 31*).

Normally, at the time of administration, drug distributors will record in their registers:

- the number of individuals who ingested the medicines;
- those who were not eligible for treatment; and
- eligible people who did not ingest the medicines for various reasons.

These data are compiled by the drug distributor for the village or urban area and sent to the IU authorities either directly or through an intermediate level. The IU authorities should ensure that data on coverage are reported by the drug distributors or peripheral reporting units immediately after each MDA campaign for compilation and calculation for that IU.

The following indicators are recommended to measure the effectiveness of MDA:

Geographical coverage indicator. The proportion of endemic IUs covered by MDA in a country or the proportion of endemic villages or urban areas covered by MDA in the targeted IU during the reported year.

$$\text{Geographical coverage of IUs} = \frac{\text{number of endemic IUs where MDA is implemented}}{\text{total number of endemic IUs where MDA is required}} \times 100$$

Sometimes MDA is not well implemented in certain parts of the IU, resulting in overall low coverage within an IU. The geographical coverage indicators below are used to better understand this kind of situation.

$$\text{Geographical coverage of villages} = \frac{\text{number of villages covered}}{\text{total number of villages in endemic IU}} \times 100$$

$$\text{Geographical coverage of urban areas} = \frac{\text{number of urban areas covered}}{\text{total number of urban areas in endemic IU}} \times 100$$

Drug coverage indicators: the proportion of individuals who actually ingested the medicines.

At the IU level, the data reported from all the drug distributors are compiled and termed the reported coverage. It is calculated on the basis of both the total population of the IU and the targeted, or eligible, population of the IU as indicated below. Reported coverage should be analysed by age group (adults aged >15 years, preschool children aged <5 years, and schoolchildren aged 5–14 years) and by sex (*32*).

$$\textit{Epidemiological drug coverage}^{4} \text{ reported in total population by IU (Programme coverage)} = \frac{\text{number of people who were reported to have ingested the drugs}}{\text{total population in IU}} \times 100$$

The epidemiological drug coverage among the total population is a reflection of what proportion of the at-risk population is being covered by MDA.

$$\textit{Drug coverage} \text{ reported in targeted or eligible, population by IU} = \frac{\text{number of people in the targeted population ingesting the MDA drugs in IU}}{\text{all individuals targeted for treatment in IU}} \times 100$$

The drug coverage in the targeted, or eligible, population is the best measure of how well MDAs were implemented. An adequate level of programme drug coverage is estimated to be 80% (*33*).

These indicators are important in enabling the IU authorities to assess the status of the elimination programme. For example, programme managers should use reported coverage data immediately to determine which, if any, areas have low coverage so that they then can investigate further and improve programme implementation.

Whereas, in most situations, the reported drug coverage should reflect the actual drug coverage, in some instances this is not the case (*34, 35*). This may be because:

- drug distributors left behind medicines for household members who were absent during their visit and recorded them as having been consumed presuming that the absentees would take the medicines on their return;
- in their enthusiasm to show good performance, drug distributors reported a higher than actual coverage;
- the data on total population or targeted population were outdated or incorrect resulting in an erroneous calculation of drug coverage. For example, the drug distributors' lists of households were less than a complete count, resulting in the denominator used to calculate reported coverage being too small.

Given the importance of achieving and maintaining high coverage in order to achieve LF elimination, reported coverage data should be verified through a

[4] Referred to as *"programme coverage" in Monitoring drug coverage for preventive chemotherapy (32).*

survey early in the programme; that is, after the second or third MDA. This provides programme managers with an opportunity to investigate reasons for low coverage and to implement remedial action if the programme failed to attain 65% coverage of the total population, the operational definition of an effective MDA.

Surveyed coverage indicator. A measure that complements and verifies the reported coverage by using population-based cluster survey methods. Surveyed coverage is calculated as:

$$\frac{\text{Total number of individuals identified by household survey as having ingested the drugs}}{\text{Total number of individuals residing in all the surveyed households about whom information on drug ingestion could be elicited}} \times 100$$

Coverage surveys provide data to compare with reported data. These data can be used, among other things, to assess the extent to which:

- treatment was directly observed;
- coverage within the targeted, or eligible, population was achieved;
- non-eligible people were included in treatment;
- non-compliant individuals exist;
- drug coverage for other NTDs was achieved.

Coverage surveys are a basic tool of programme management permitting the identification and correction of problems. After each MDA round, if coverage surveys cannot be done in all IUs, they could be done in one or two sites within one or more IUs, and conducted in different IUs each year. In each IU, the surveyed coverage should be carried out at least once during the course of the programme and more frequently if resources are available; however, it does not have to be done after every round of MDA. The surveyed coverage should be carried out by an independent team from outside the IU.

Annex 4 describes how to conduct MDA coverage surveys using a survey design similar to one often used in surveys of immunization coverage (*36*).

Table 2 shows how to interpret and follow-up the results of reported and surveyed coverage.

Finally, at the national level, the *WHO manual on Monitoring drug coverage for preventive chemotherapy* recommends calculating an additional indicator, national coverage, after each round of MDA (*32*). National coverage is the proportion of individuals in an endemic country requiring MDA for LF who have ingested the appropriate medicine as part of a preventive chemotherapy package.

National coverage is defined as:

$$\frac{\text{Number of individuals ingesting MDA drugs for a specific disease in an endemic country}}{\text{Number of individuals at the national level requiring MDA for a specific disease in an endemic country}} \times 100$$

Table 2. Interpreting and following up reported and surveyed coverage results

Finding or observation	What to look for	Corrective action
Reported coverage and surveyed coverage are both low	Check the geographical coverage of areas within the IU to see if any areas are being left uncovered. Check for coverage in the different age-groups (<2 years, 2–5 years, 6–14 years and >15 years) to determine whether any particular age-group is being left out. Check the reasons for the eligible population not taking the drug. May need a special Knowledge, Attitude and Practices (KAP) survey in the population to assess the problem.	Depending on the problem, may require MDA in the areas not yet covered in the IU. Improve social mobilization of communities. Improve the skills and motivation of drug distributors by better training and supervision.
Reported coverage is much higher than surveyed coverage	Drug distributors incorrectly reporting on ingestion of medicines. Figures on total population and eligible population are incorrect or outdated, or people from outside the IU are also taking the drugs from the drug distributors and are being recorded as residents of the IU.	Improve the skills and motivation of drug distributors by better training and supervision. Ask the drug distributors to record and report the non-resident individuals ingesting the medicines separately. Do not include them in the numerator for calculating the drug coverage for the IU.
Reported coverage is much lower than surveyed coverage	Figures on total population and eligible population are incorrect or outdated.	Update and correct population data.
Both reported coverage and surveyed coverage are high	A good reporting system is in place. Communities and drug distributors are motivated. All elements of the MDA programme are well in place and functional.	Sustain programme momentum for the next year to maintain coverage levels.

6 Assessing the impact of mass drug administration through sentinel and spot-check sites

The impact of MDA is assessed through sentinel and spot-check sites to provide programme managers with reasonably accurate information on the trend of the infection over the course of the programme.

6.1 What geographical area should be used to assess impact?

Full-scale assessments of a programme's impact are required to make decisions about whether to alter control efforts. These are expensive and cannot be done frequently. It is recommended that a small number of sentinel and spot-check sites be assessed and the results used to decide whether a full-scale assessment is warranted. The choice of sentinel and spot-check sites depends on the country situation. While the following section gives general guidance, it is recommended that programme managers discuss and seek advice on what is appropriate for their situation through the RPRGs and meetings of programme managers.

6.1.1 Choice of sentinel and spot-check sites

Before the first round of MDA is implemented in the IU, the sentinel site(s) for that IU need to be identified. These sites will be used to ascertain the baseline parasitological indicators and will make it possible to carry out periodic evaluation of these indicators.

Ideally, each sentinel site should collect data from 300–500 individuals aged over 5 years. The size of the population screened is not determined on statistical grounds as it is intended as a convenience sample of a group chosen because they are considered to be at high risk. In addition, because adults, who generally have a higher prevalence of microfilaraemia than children, are included in the screening, the decision criteria for implementing a survey to assess transmission is considered conservative (see section 7.2).

6.1.1.1 Characteristics of sentinel sites

The characteristics required of a sentinel site are as follows:

- a population of at least 500 people (in order to collect samples from at least 300 people);
- chosen from an area of known high transmission (high disease or parasite prevalence or vector abundance) or from an area where difficulty in achieving high drug coverage is anticipated. These are the areas within the IU likely to require the longest period of time for interruption of transmission. However, if specific transmission data do not exist, the sentinel site should be chosen using the best information available;
- no prior MDA for onchocerciasis;
- a stable population that is not affected by migration and with the same demographic characteristics as the IU as a whole.

Once chosen, the same site should act as the sentinel site throughout the course of the programme.

6.1.1.2 Characteristics of spot-check sites

Spot-check sites have the same characteristics as sentinel sites but, unlike the sentinel sites, which remain the same over the course of the programme, different spot-check sites are chosen for every assessment. Spot-check sites provide additional information on the prevalence of microfilaraemia in the IU and are important to counteract any potential sentinel site bias (*37, 38*). They should be in an area considered at high risk for continued transmission. At least one spot-check site should be chosen per sentinel site, and more if resources permit.

6.1.2 How many sentinel sites are needed for each implementation unit?

The greater the number of sentinel sites, the greater the expense, but also the more likely that the data collected will be representative of the IU. At least one sentinel site should be identified for each IU. If resources permit, especially if the IU is large, two or more might be chosen. While there is no strict rule, it is recommended that, at minimum, there be at least one site per 1 000 000 population in the IU.

Very small IUs, however, might be combined to be serviced by one sentinel site. When grouping IUs for the common reference sentinel sites, the IUs should be in geographical proximity, share similar epidemiological characteristics and should all implement MDA at the same time. Decisions based on the epidemiological trend

in the common reference sentinel sites would be applicable to all IUs in the group and not only to the IUs in which sentinel sites are located. As this arrangement is an exception to the usual procedure, the advice of WHO and the RPRG might be required.

6.2 When should assessment occur?

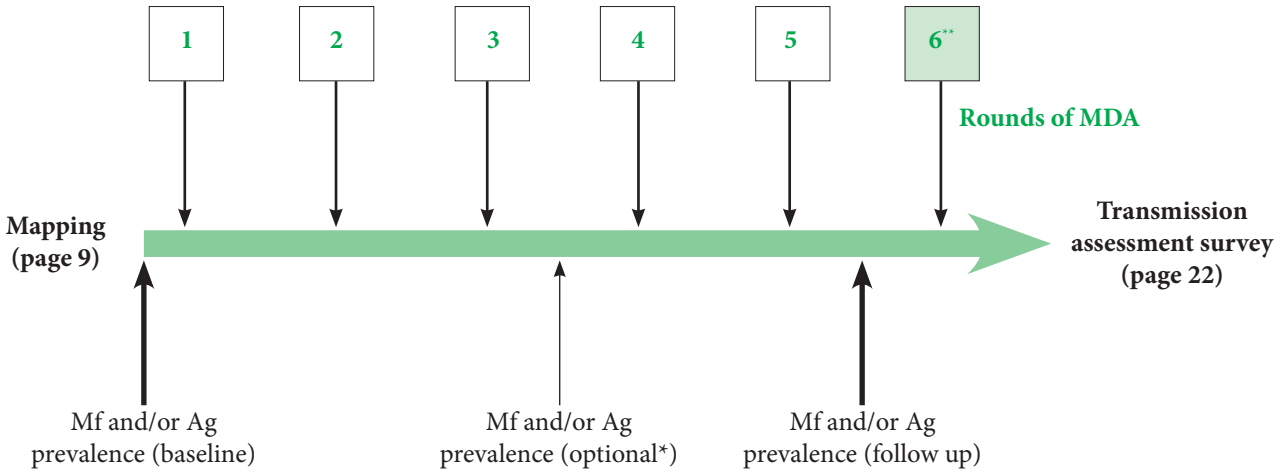
To collect baseline information on prevalence of microfilaraemia, data should be collected in sentinel and spot-check sites before the first round of MDA (*Figure 2*). Baseline collection is done to validate mapping results, as well as to provide a level with which to compare later monitoring results.

Where resources are available and programme managers believe it would be helpful for monitoring the progress of programmes, sentinel and spot-check sites can collect data at least 6 months after the third round of MDA (*30*). These mid-term results can be used both to ensure that drug coverage results are accurate, that is, that drug coverage is adequate enough to lead to decreased prevalence of infection, and to provide data for advocacy and motivation of staff.

Data should also be collected at least 6 months after the fifth round of MDA to be used for two reasons: (i) to track a programme's impact by comparing its baseline and mid-term results; and (ii) to assess whether the TAS should be implemented (see section 7.2).

If after the TAS is implemented, results show that infection levels have not been lowered to a point where transmission is likely no longer sustainable, MDA should continue, and sentinel and spot-check site data should be collected every 2 years until the criteria for stopping MDA have been met.

Figure 2. Timing of sentinel and spot-check site assessments in national programmes



Mf = microfilaraemia; Ag = antigenaemia; measured by ICT; * Could be replaced by effective annual monitoring of coverage; ** Likely, but not necessary, to be conducted no matter assessment results.

6.3 How should assessment be implemented?

6.3.1 Target population

Both sentinel and spot-check sites should have populations of at least 500 people, so that samples can be collected from at least 300 people. The population should be similar to that of the IU (e.g. farmers, fishermen or city dwellers). All members of the population of the sites should be included, or, where the population is too large, a part of it can be chosen. Children aged >5 years, as well as pregnant women, should be included in the assessment, with samples being collected from all age groups aged >5 years.

In rural areas, a county, village, hamlet or a subdistrict can be chosen, whereas in cities or towns, boroughs or wards can be chosen.

6.3.2 Diagnostic tools

At this time, it is recommended that programmes use microfilaraemia prevalence in sentinel and spot-check sites in order to measure ongoing transmission. Because microfilaraemia prevalence decreases dramatically after MDA, measuring its prevalence can provide evidence of the effectiveness of the MDA (*39*).

If resources allow, programmes can collect information on antigenaemia using ICTs in sentinel and spot-check sites. Antigen rates decrease more slowly than microfilaraemia rates, so will underestimate the effects of MDA, particularly after the first few rounds (*24, 40, 41*). People with positive ICT results could be followed up with microfilaraemia testing, as these data would help inform operational research on the relationship between microfilaraemia and antigenaemia in areas with MDA. In addition, programme managers can collect simple information in sentinel sites on clinical manifestations, MDA coverage and compliance issues.

6.4 How does this approach relate to an integrated strategy control of neglected tropical diseases?

In areas where LF and other NTDs are endemic, the prevalence of other diseases could be assessed in sentinel and spot-check sites, for example, by collecting stool samples from the population targeted for STH and/or schistosomiasis interventions. Indicators of cross-cutting impact, such as those for anaemia, disability and blindness, also could be added to data collection from sentinel and spot-check sites where appropriate (*42*). Information such as prevalence of clinical manifestations and compliance with MDA could be collected through integrated surveys such as those asking about bednet usage in areas where malaria is co-endemic.

7 Transmission assessment surveys

Evaluation is necessary to determine whether the programme has achieved its objective of reducing levels of microfilariae in endemic populations to an extent where transmission is likely no longer sustainable. Programmes must be able to assess whether MDA has succeeded in lowering the prevalence of infection to a level where recrudescence is unlikely to occur.

Transmission Assessment Surveys (TAS) are designed to help programme managers determine whether areas have reached this critical threshold of infection (*43*). The *Survey sample builder* tool[5] can be used to automate the calculations for determining the appropriate survey strategy. The design of the TAS is flexible in order to best fit the local situation; it depends upon factors such as the net primary-school enrolment ratio, the population size, the number of schools or enumeration areas and the feasibility of different survey methods.

While the TAS provides helpful evidence to national programmes regarding the decision to stop MDA, programme managers must thoughtfully consider the decision about whether to stop or to continue MDA.

7.1 What geographical area should be used?

The study area selected for the TAS will be designated as an evaluation unit (EU), which may comprise multiple IUs or part of an IU. IUs within an EU can, but need not be, geographically contiguous, but they all should have had at least five effective MDA rounds and share similar epidemiological features, such as rates of MDA coverage and/or microfilaraemia prevalence in sentinel and spot-check sites.

Combining IUs into a single EU reduces overall survey costs but carries with it some risks. For example, if the critical threshold is exceeded, all IUs that comprise

[5] The *Survey sample builder* tool is available at http://www.filariasis.us/resources.html.

the EU will have to continue MDA. Another risk is that the EU passes even though the prevalence of infection in one or more IUs is above the threshold, potentially allowing transmission to recrudesce in these IUs. In general, EUs should have no more than 2 million people, in order to increase the confidence that transmission is no longer sustainable in the surveyed area.

7.2 When should surveys occur?

All IUs within the EU must have completed five "effective" rounds of annual MDA. To be considered effective, these MDAs should have rates of drug coverage exceeding 65% in the total population.

An assessment after the fifth MDA using blood films should be carried out no sooner than 6 months after the MDA in all ages greater than 5 years in sentinel and spot-check sites. The results of the assessment should show the prevalence of microfilaraemia to be <1% in all sites in order to continue to implementing the TAS.[6]

Given the lead times required to have medicines available and to make preparations for an MDA, it will generally be necessary to conduct the sixth round of MDA, regardless of the results of the sentinel and spot-check site assessment.

In EUs that have met the above criteria, programme managers should plan to conduct the TAS at least 6 months after the last MDA round.[7]

7.3 How should the surveys be implemented?

7.3.1 Target population

Children aged 6–7 years should be surveyed because they should be protected from LF infection if the MDAs have been successful in interrupting transmission.

Antigenaemia in young children is a marker for relatively recent events of transmission, while antigenaemia in older children or adults may be related to infections that occurred before MDA. For school-based surveys, first- and second-year primary-school children can be used to approximate the study population, realizing that there may be a few children outside of these ages. Community-based household surveys should specifically focus on children aged 6–7 years in the selected households.

Where there has been no evidence of filarial transmission for many years, the school level of children among whom filarial antigenaemia is measured can be matched with the epidemiological profile of exposure to filarial infection in the IU and a wider age range could be considered.

---

[6] For sites using ICTs to measure antigen prevalence, all sites should show <2% prevalence in order to continue to implementing the TAS.

[7] The next round of MDA should not be planned until the results of the TAS are known. If the evaluation unit fails the TAS, then the next round of MDA is planned. While following this guidance might result in a gap of a year between MDA rounds, it assumes that the majority of evaluation units will pass the TAS.

7.3.2 Diagnostic tools

In areas where W. bancrofti is endemic, ICT tests should be administered to all surveyed individuals to measure levels of antigenaemia. ICTs require no laboratory equipment and can be processed quickly. A positive result indicates the presence of adult worms and therefore is a measure of the potential for ongoing transmission. ICTs are simple to use, but training is required to ensure that cards are not misread, which most often leads to false-positive results, and that different readers agree on the results. Programmes also should implement quality control of the ICTs before use. Annex 2 provides more information on quality control and use of ICTs. If such tests are not available, the programme can collect serum samples for ELISA testing in a laboratory.

In areas where Brugia spp. is endemic, the Brugia Rapid™ test should be administered to all surveyed individuals to measure levels of antibody (*Annex 3*). If the Brugia Rapid™ test is positive, programme managers can choose to do follow-up testing for microfilaraemia at night during the hours of peak microfilariae circulation. These data will help better define the relationship between antibody and microfilaraemia positivity. If such tests are not available, the programme can collect serum samples for ELISA testing in a laboratory.

In areas endemic for both *W. bancrofti* and *Brugia spp*., both diagnostic tools should be used. Positive results from ICT and Brugia Rapid™ testing should be evaluated separately against the critical cut-off thresholds.

7.3.3 Survey design

The survey design is derived from the methodology outlined in the Manual for survey planners and is summarized below (*43, 44*). The following survey design is intended for implementation in EUs that are known to have been previously endemic for either *W. bancrofti* only or *Brugia spp*. only. In areas where *Anopheles* or *Culex* is the principal vector, the methodology follows the algorithm in *Figure 3*; in areas where *Aedes* is the principal vector, the methodology follows the algorithm in *Figure 4*. For EUs where parasite species overlap, please refer to *Annex 5*. For countries or EUs with small populations, the survey design may need to be modified to be more feasible to implement. In these cases, consultation with WHO and technical experts is advised.

7.3.4 Survey sites

School-based survey. If the net primary-school enrolment ratio[8] is greater than or equal to 75% in the EU, the schools will be the survey sites and first- and second-year primary school students will be the survey population.[9] While 6–7 year-olds are the target population, this age requirement can be cumbersome, so all children in these classes will be eligible for sampling. In these areas, it is advisable also to consider the

[8] Net primary-school enrolment ratio is the number of children enrolled in primary school who belong to the age group that officially corresponds to primary schooling, divided by the total population of the same age group (http://www.unicef.org/infobycountry/stats_popup5.html). In some countries, the admission ratio, that is, the net first-year enrolment ratio, may be available. If so, this would be the more useful indicator for the decision-making algorithm.

[9] The 75% threshold proposed in this manual is used as a level for deciding whether to conduct school-based surveys or community-based surveys. The results of ongoing operational research will determine whether this distinction should be maintained (that is, whether significant differences exist between infection levels in children attending school and those who do not).

Figure 3. Algorithm for choice of Transmission Assessment Survey (TAS) design in areas where *Anopheles* or *Culex* is the principal vector

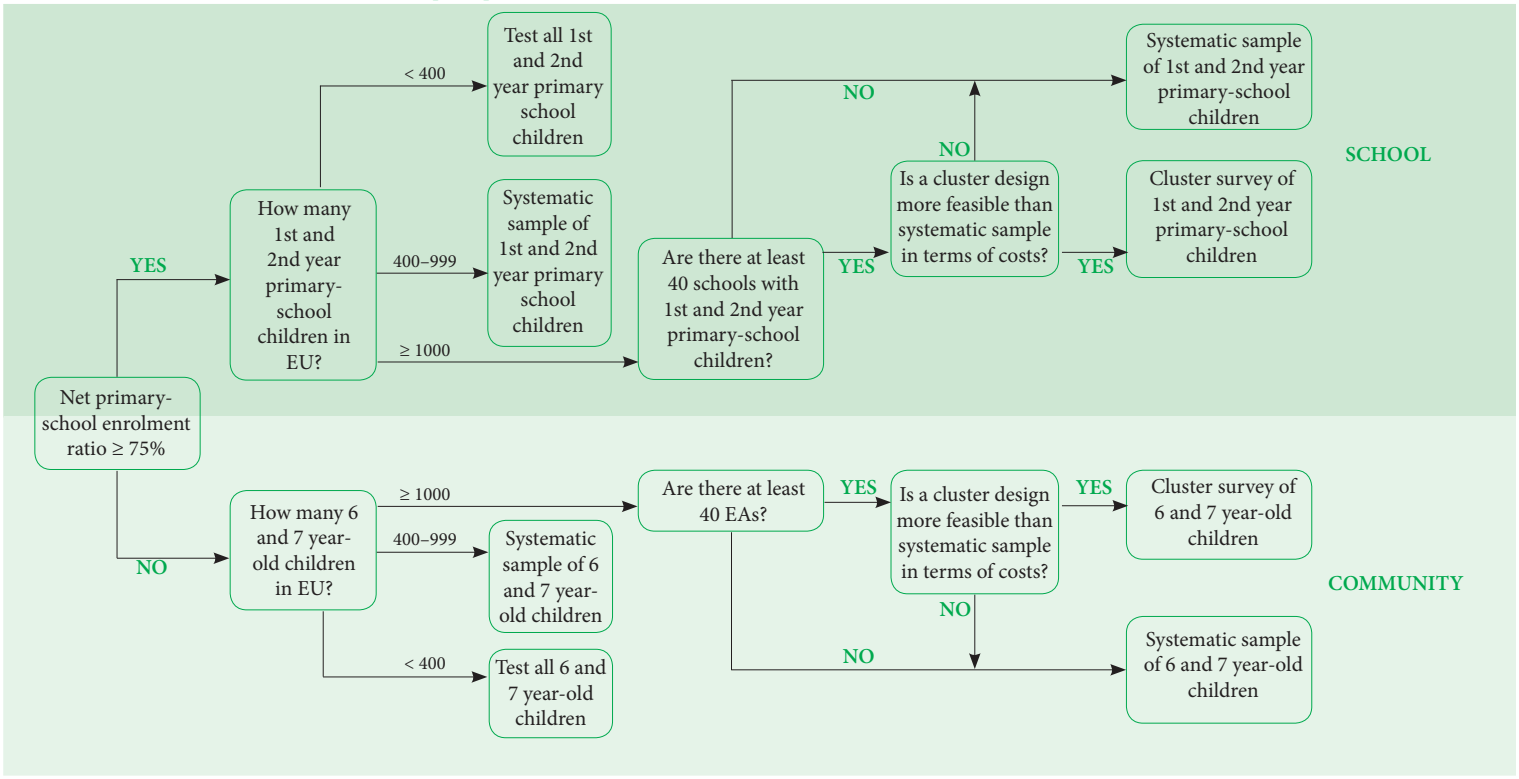
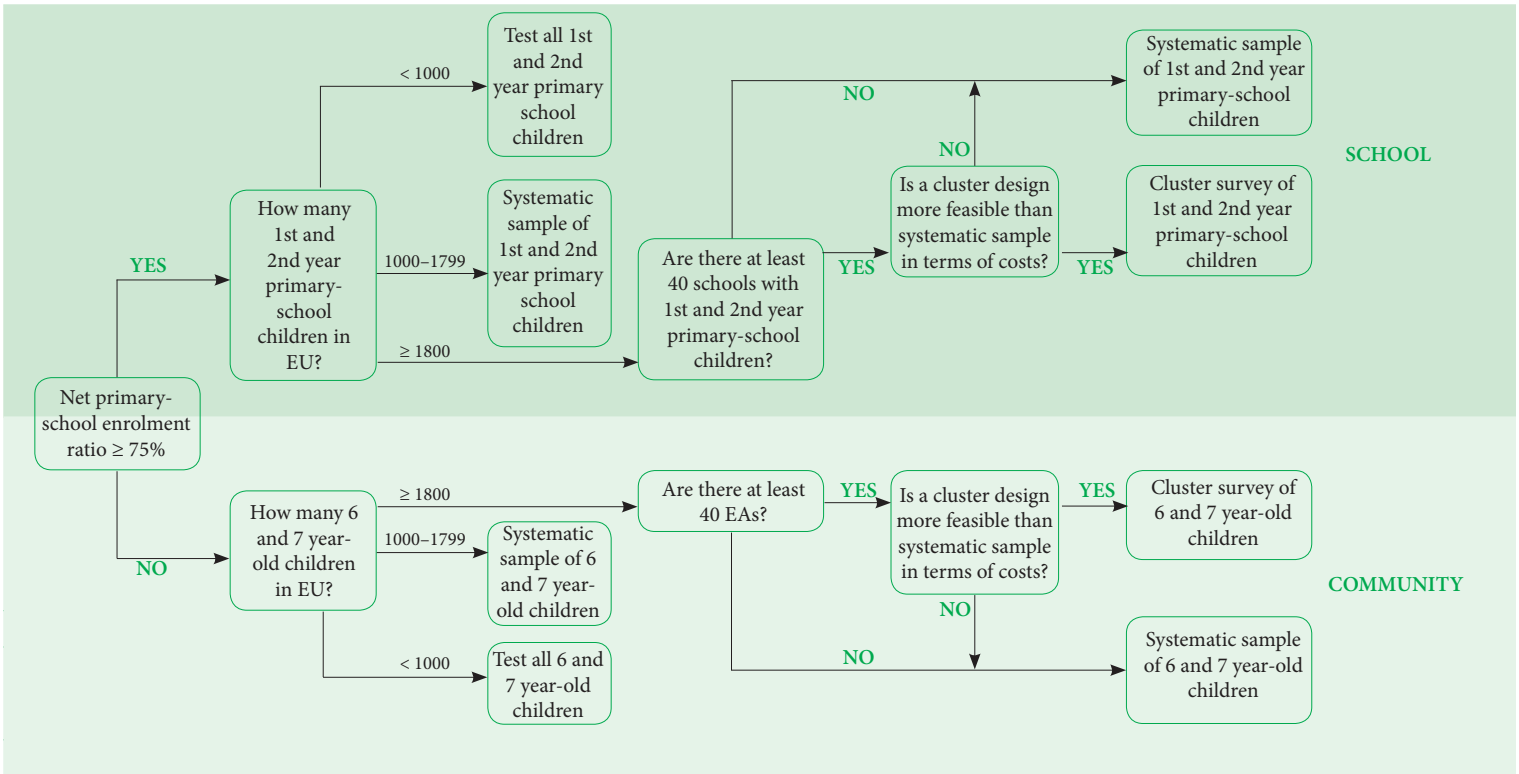


Figure 4. Algorithm for choice of Transmission Assessment Survey (TAS) design in areas where *Aedes* is the principal vector



characteristics of the school-age population who do not attend school. Where there is evidence that rates of school absenteeism are high in communities thought to be at high risk of LF, a community-based survey should be considered.

Community-based survey. In areas where the rate of school enrolment is below the 75% threshold, census EAs are recommended as clusters if cluster-sampling is used. EAs are usually the smallest area for which census population results are available. It is important to note that although village might be designated as an individual EA, the definitions are not interchangeable. One EA may include more than one small village. Larger villages may also be divided into more than one EA. The survey teams need to learn to use the EA maps or work with the census office.

Community-based household surveys are more expensive and time consuming than school-based surveys. However, if less than 75% of children are enrolled in schools, implementing school-based surveys could potentially introduce selection bias, which could lead to statistically significant differences in rates of infection between children attending school and those who do not.

7.3.5 Survey population

School-based survey. For school-based surveys, all children *enrolled* in the first or second year of primary school should be considered eligible for the survey sample. Although a small number of this survey population may fall outside the intended target age of 6–7 years, it would still encompass children born after the start of MDA. Extreme outliers (children aged >10 years) should be included in the data collection, but may be excluded during data analysis if warranted.

School enrolment data (the number of first- and second-year primary-school children and the list of all primary schools in the EU) and average absentee rate for this group should be obtained with assistance from the Ministry of Education. Where this number is not attainable, it may be estimated through census population data and the expected rate of primary-school enrolment.

Community-based survey. For community-based household surveys, the total number of children aged 6–7 years in the EU (using data from the national census bureau) is eligible for inclusion. If census data exist only for 5–9-year-olds, it is reasonable to approximate 40% for the proportion of 6–7-year-olds. Data projected from the most recent census should factor in the average projected annual population growth rate.

Census. In areas where *Anopheles* or *Culex* is the principal vector, if the total target population is less than 400, samples should be collected from all children aged 6–7 years or all first-and second-year primary-school children. Similarly, in Aedes areas, if the total target population is less than 1000, a census should be conducted.

7.3.6 Survey strategy

For both community-based household surveys and school-based surveys, children will be selected using a cluster-sample design or directly by systematic sampling. The choice between these sampling methods depends on the number of 6–7-year-olds and on the number of clusters (schools or EAs) in the EU. Sample sizes are smaller with systematic sampling, but survey teams may need to visit all EAs or schools. Sample sizes for cluster-sample surveys are larger, but only a subset of schools or EAs needs to be visited. For both sampling methods, the recommendation to stop or continue MDA will be based on whether or not more than a critical number of antigen-positive or antibody-positive children have been identified in the sample. Both methods, therefore, are examples of lot quality assurance sampling (LQAS). The *Survey sample builder* tool[10] can be used to automate the calculations for determining the appropriate survey strategy.

7.3.7 Sample size calculations

The sample size needed for surveys is found in the *Manual for survey planners* (and as *Tables 1* and *2* in *Annex 5*). The *Survey sample builder* tool can also be used to automate sample size calculation.

In areas where *W. bancrofti* is endemic and *Anopheles* or *Culex* is the principal vector, the target threshold is <2% antigenaemia prevalence. The sample sizes and critical cut-off values were chosen so that an EU has:

1) at least a 75% chance of passing if the true prevalence of antigenaemia is 1.0% (half the target level); and
2) no more than about a 5% chance of passing (incorrectly) if the true prevalence of antigenaemia is ≥2%.[11]

Because Aedes species are known to be more efficient transmitters of the parasite, it is hypothesized that the prevalence of infection in the population needed to sustain transmission is lower than in areas with different principal vectors (*21*). Therefore, in Bancroftian areas where *Aedes* is the primary vector, the target threshold is half of that in areas where *Anopheles* or *Culex* is the main vector, that is, <1% antigenaemia prevalence. The sample sizes and critical cut-off values in *Aedes* areas were chosen so that an EU has:

1) at least a 75% chance of passing if the true prevalence of antigenaemia is 0.5% (half the target level); and
2) no more than about a 5% chance of passing (incorrectly) if the true prevalence of antigenaemia is ≥1%.[12]

[10] The *Survey sample builder* tool is available at http://www.filariasis.us/resources.html.
[11] The reason is that Ag prevalence is always higher than Mf prevalence; therefore the <2% prevalence target for Ag is used as a conservative proxy for an Mf prevalence of <1%.
[12] The reason is that Ag prevalence is always higher than Mf prevalence; therefore the <1% prevalence target for Ag is used as a conservative proxy for an Mf prevalence of <0.5%.

In areas where *Brugia spp*. is endemic, the target threshold is <2% antibody prevalence. The sample sizes and critical cut-off values were chosen so that an EU has:

1) at least a 75% chance of passing if the true prevalence of antibody is 1% (half the target level); and
2) no more than about a 5% chance of passing (incorrectly) if the true prevalence of antibody is ≥2%.

7.3.8 Cut-off criteria

The TAS is designed to give programme managers a critical cut-off value. If the number of antigen-positive or antibody-positive results found is no more than this number, the EU "passes" and it is assumed that transmission can no longer be sustained, even after MDA has been stopped.

In areas endemic for *W. bancrofti*, if the number of ICT (antigenaemia) positive children tested is less than the critical cut-off number found in *Tables 1* and *2* in *Annex 5* or in the *Manual for survey planners*, it is likely that transmission can no longer be sustained. Governments can decide to stop MDA in the EU. If the number of positive children is greater than the critical cut-off number, MDA should continue in the EU for two more rounds.

In areas where Brugia spp. is endemic, the number of Brugia Rapid™ (antibody) positive children will use the same critical cut-off values as in *W. bancrofti* areas with *Culex* or *Anopheles* vectors. While it is recognized that antibody levels will most likely be higher than antigen levels (*25, 46, 47*) and this threshold might be conservative; further operational research is still needed to define the precise relationship between antibody prevalence in children and sustainability of transmission.

The following boxes include examples of survey design and cut-off levels for school-based and community-based surveys. *Annex 5* includes more detailed information on implementing the TAS, including suggestions on treatment and follow up of ICT or Brugia Rapid™ positive test results.

School-based survey – Example 1

- Principal vectors: *Anopheles* and *Culex*
- 20 000 first- and second-year primary-school children enrolled in the evaluation unit = survey population
- 400 total primary schools
- From Table 1 of the *Manual for Survey Planners* and row for population = 18 000
  - Sample size = 1552 first- and second-year primary-school children
  - Number of clusters in survey sample = 32
  - All first- and second-year primary-school children included in the survey sample in each of the 32 selected schools
  - Critical cut-off = 18

School-based survey – Example 2

- Principal vector: *Aedes*
- 1250 first- and second-year primary-school children enrolled in the evaluation unit = survey population
- 35 primary schools
- From Table 2 of the *Manual for Survey Planners* and row for population = 1200
  - Sample size = 730 first- and second-year primary-school children
  - Systematic sampling (not cluster sampling) survey design
  - Critical cut-off = 4

Community-based household survey – Example 1

- Principal vectors: *Anopheles* and *Culex*
- 25 000 6–7-year-olds in the evaluation unit = survey population
- 325 total enumeration areas
- From Table 1 of the *Manual for survey planners* and the row for population = 24 000
  - Sample size = 1556
  - 30 clusters (enumeration areas) in the sample
  - A sample of 6–7-year olds selected within each of the 30 enumeration areas
  - Critical cut-off = 18

Community-based household survey – Example 2

- Principal vector: *Aedes*
- 71 000 5–9 year-olds in the evaluation unit according to census projections
- Estimated survey population ~= 40% x 71 000 = 28 400
- 418 total enumeration areas
- Average number of 6–7-year-olds per enumeration area: 28 400/418 = 68
- From Table 2 of the *Manual for survey planners* and the row for population >18 000
  - Sample size = 3080 6–7-year-olds
  - Enumeration areas in sample = 3080/68 (rounded up) = 46
  - Critical cut-off = 18

8

Implementing activities and surveillance after mass drug administration has stopped

8.1 What other activities will be implemented after MDA has stopped?

Even after MDA has stopped, the LF elimination programme will continue. National programmes will need to develop plans that include activities to manage morbidity and prevent disability, as well as ongoing surveillance and evaluation. Post-MDA activities will occur in each evaluation unit as individual units stop MDA and then at a country level, once the entire country has stopped MDA.

Post-MDA activities will vary according to the country situation. Some countries might implement a policy of "testing and treating" for high-risk populations such as migrants. Under this policy, positive cases would be treated with a single dose of DEC and albendazole or ivermectin and albendazole. If such cases can be followed up easily, repeat testing and treatment if positive could be done. Other countries might continue with vector control measures to ensure that recrudescence will not occur.

Programmes should aim to integrate post-MDA surveillance activities with those of other NTD control programmes, or integrate LF surveillance activities with population-based surveys to minimize the need for long-term resources for LF-specific surveillance (*42*). This would be useful both in between the TAS (see section

8.2.1), as well as after the final surveys have been completed. National surveys such as DHS (demographic and health surveys) might also be used to collect post-MDA surveillance data.

8.2 What type of surveillance should be implemented?

Surveillance after MDA has stopped can be implemented in two ways: (i) periodic surveys; and (ii) ongoing surveillance activities, which are advantageous to start as soon as possible, including while MDA is ongoing.

8.2.1 Periodic surveys

Repeating a TAS is the best option for periodic surveys during post-MDA surveillance. A series of two post-MDA surveillance surveys should be conducted to evaluate whether recrudescence has occurred. Each survey should be conducted approximately 2–3 years following the previous survey and should use a similar design as the original TAS (*Figure 5*).

The timing of a repeat survey has no single best choice for all programmes. When MDA has been stopped despite concerns that transmission may not have been extinguished, a second survey conducted after 2 years might be preferred to detect any early signs of recrudescence. A longer interval is more likely to identify recrudescence and might be preferred for programmes in which all indicators for success of MDA have been achieved. Three years might be chosen by such programmes to reduce problems caused by staff attrition or loss of programme visibility.

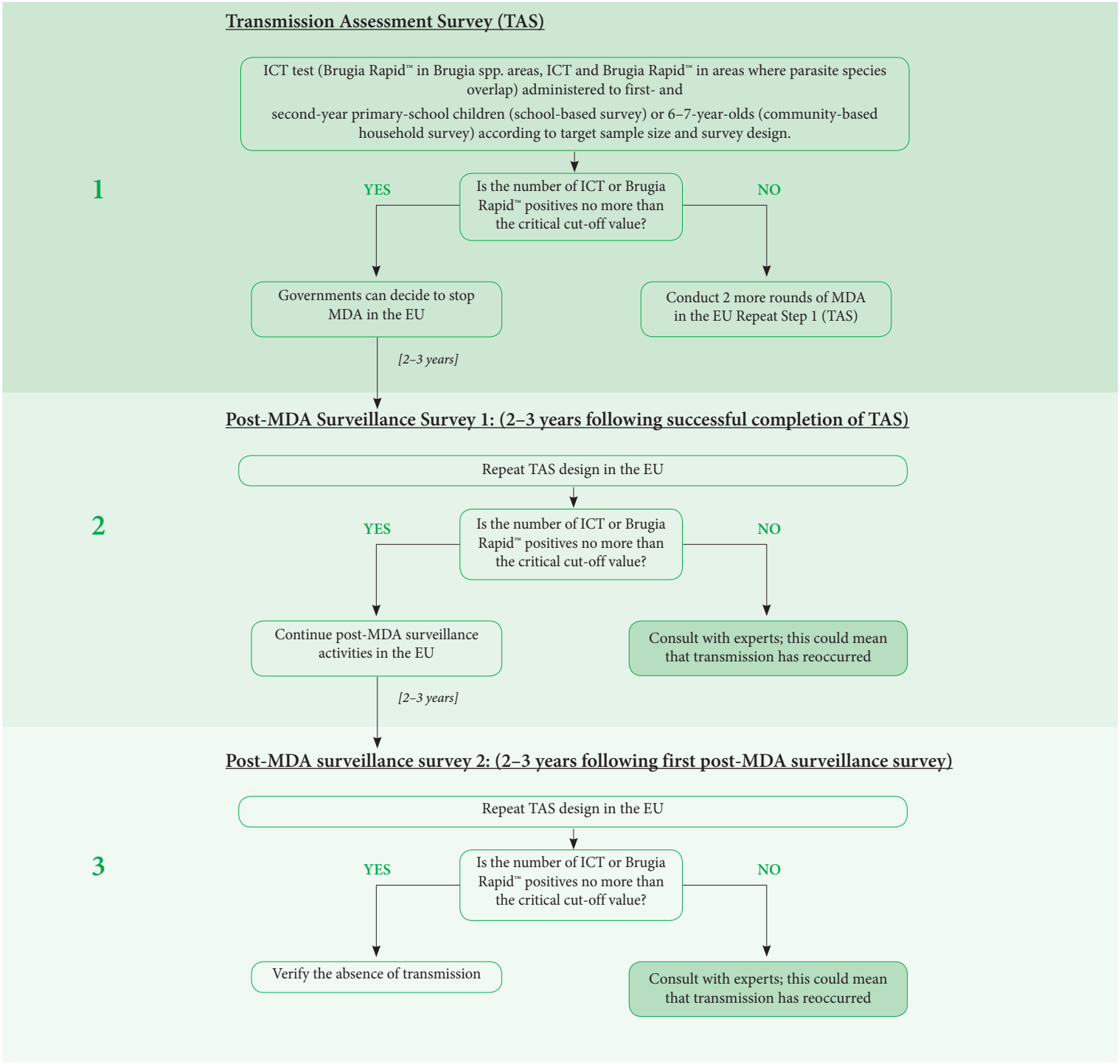
Comparing antigen-positive or antibody-positive cases to the critical cut-off is more important than comparing differences between the first and second surveys. If the post-MDA surveillance survey results are greater than the critical cut-off point, this could be a warning that transmission has resumed. It is important to consult with WHO, the RPRG, and/or other experts in order to decide on next steps. Depending upon the level of antigenaemia or antibody detected during these surveys, additional rounds of MDA might be required. Reassessment of the MDA stopping criteria could be repeated after one or more additional rounds of MDA.

8.2.2 Ongoing surveillance

National programmes should implement ongoing surveillance to detect new foci of transmission, collect data on infection trends in the general population and confirm the interruption of transmission. Ongoing surveillance should cover the entire country, except in areas with no risk of transmission (for example, areas at high altitudes where no vectors are present). The following population groups can be surveyed:

- military recruits (during their medical check-up);
- university students (during their medical check-up or prenatal examination);
- blood donors;
- hospitalized patients.

Figure 5. Transmission Assessment Survey (TAS) and post-MDA surveillance survey flow



Clinical laboratories (for malaria, tuberculosis or HIV) at hospitals could be asked to test a certain number of blood samples a month for the presence of microfilaraemia, antigenaemia, or antibodies. This information could be reported to the national programme and other disease control programmes. If any positive cases occur, they could be treated directly at the hospital, but also investigated by staff of the national programme to determine the source of infection.

8.3 What other potential future surveillance strategies are available?

Two additional approaches to post-MDA surveillance for *W. bancrofti* transmission depend on diagnostic tools that are not yet fully developed or standardized.

The first is the use of an antibody assay reflecting exposure to infective larvae (whether or not infection is established). Antibody assays are currently being field tested and information is being collected on the comparison of the results of antibody tests with other diagnostic tests (*37, 47, 48*).

The second is direct assessment through PCR techniques of parasites in vector mosquitoes, that is, xenomonitoring (*49–51*). While molecular xenomonitoring can be used to measure microfilaraemia prevalence in a community, there is a need for research to develop more feasible methods for sampling and testing.

These approaches often rely on the availability of national or regional reference laboratories, in contrast to the ICT point-of-care assay currently used for surveillance. As progress in developing and validating these approaches has been good, it is anticipated that at least one of these new diagnostic tools will become available for use in post-MDA surveillance in the near future.

9 Verifying the absence of transmission

9.1 Background

In 1993, the International Task Force for Disease Eradication identified LF as one of only six infectious diseases "that possibly could be eradicated" (*52*). In 1997, the World Health Assembly called for the "global elimination of lymphatic filariasis as a public health problem" (resolution WHA50.29). Although the Task Force considered LF to be potentially eradicable, GPELF was established with the goal of global *elimination* of LF, rather than its *eradication*. Although there may be no biological distinction between these terms (only a geographical one, with eradication implying global elimination), by convention, disease eradication programmes require formal certification processes, which are both costly and time-consuming. No such certification process has been established for LF elimination. However, there is a critical need to establish a process for external evaluation of the evidence for elimination and for official recognition of the success. The process for such recognition is called "verification of the absence of transmission".

For the purposes of this verification procedure, absence of LF transmission is defined as reducing transmission of the parasite to a level where continued transmission (and recrudescence) is not expected. Filariasis transmission involves both humans and mosquitoes; it is not directly observed except in experimental settings, and is influenced by vector, human and parasite densities. The precise threshold below which infection cannot be sustained has not been defined except in specific settings (for example, in China under conditions of mass treatment and intense surveillance) (*WHO/WPR 2004*). Therefore, tentative *indicators* of transmission have been developed based on the prevalence and intensity of filarial infection in humans. Currently, for LF programme managers, this transmission threshold is thought to have been reached if the prevalence of the infection among surveyed children is below the threshold defined in the TAS protocols described in section 7.

TAS surveys are considered important evidence that transmission has been interrupted (or the threshold reached); however, in isolation from other factors such surveys are insufficient for verification. Rather, it is important that each country requesting verification of absence of LF transmission present detailed historical and epidemiological evidence that transmission has been interrupted, including a description of ecological factors that favour the interruption of transmission and the adequacy of surveillance to detect recrudescence.

Although verification of absence of LF transmission does not include information on individuals with filarial disease, care of people with LF-associated morbidity is a stated goal of the programme. Therefore, if available, data on filarial disease and available treatment should be presented as part of the dossier.

9.2 The dossier

The dossier should present systematically the evidence for absence of LF transmission for the entire country. Geographically separate foci should be dealt with separately.

Terms that are used at a national level that may not be understood internationally should be defined (e.g. "imported case", "endemic district").

Spatial presentation of data is encouraged. At a minimum, maps should be included that show each IU, as well as a national-level or regional-level map indicating endemic and non-endemic areas.

The following section contains general guidance on what to include in a dossier and should be adapted to specific country circumstances based on past history and epidemiology.

Dossier contents

1. General description

The general description should focus on:

- geographical and economic features of the country, particularly as they relate to risk of LF transmission;
- the health system, emphasizing the adequacy of the health system to detect cases of infection and provide treatment;
- geographical distribution, feeding behaviour, density and competence of the vector mosquitoes;
- immigration patterns to and from LF-endemic areas (including other countries);
- occurrence of LF in neighbouring countries and the status of filariasis control or elimination efforts in those countries.

2. History of lymphatic filariasis

- A detailed description, including maps of historic foci of LF transmission, as documented by both government and research efforts. This should include a review of data on prevalence and intensity of LF infection in humans and vector mosquitoes.
- Evidence for the absence of LF transmission in areas considered to be non-endemic. Information should be provided on how non-endemic areas were defined and on surveillance in these areas to provide assurance that they remain non-endemic.
- A description of filarial disease, including geographical distribution, prevalence and treatment for its various clinical manifestations.

3. Interventions

- A detailed description of all measures to control or interrupt transmission in each focus. This description should include details of screening, testing and treatment of patients who test positive, MDA and ancillary measures, such as environmental and economic improvement, vector control and other relevant interventions, such as elimination or control activities targeting other vector-borne diseases (e.g. malaria).
- Review of case management for filarial disease.

4. Assessment of interventions

- A detailed description of surveys and studies conducted to evaluate the impact of the interventions (e.g. microfilaraemia surveys). This chapter would include data from sentinel sites and surveys for antigenaemia, as recommended by WHO, as well as other surveys or evaluations that have been conducted before the GPELF was established. It also would include any sampling undertaken as part of the decision to stop MDA or other interventions.
- Details should be provided on sampling methods and procedures that were used to assess baseline prevalence, monitor the programme and assess stopping points for MDA.
- Review of any data collected on the impact of interventions on filarial disease.

5. Surveillance

- A full review of any surveillance activities undertaken since MDA and other interventions were stopped, including TAS, other active surveillance activities, and a description of case follow-up activities completed for each positive case detected.
- Review of data collected through post-MDA surveys, such as the TAS.
- Review of the filariasis case reports through routine disease surveillance or other systems for case detection.
- Evidence that adequate sampling or surveillance was conducted in all previously endemic areas and in areas that were defined as non-endemic during initial mapping.

- Details on surveys done in cross-border areas and in immigrants from filariasis-endemic areas (e.g. date of surveys, number of people tested, test results, follow-up of any microfilaraemia-positive cases).
- Demonstration that any positive cases detected following MDA represented isolated events not traceable to an area of active transmission. If an area of potential transmission was discovered, evidence should be presented that subsequent interventions (e.g. MDA) were successful.

6. Additional data that support the absence of LF transmission.

7. Bibliography

- Published and any available unpublished studies on LF, its geographical distribution and control, including theses and dissertations.

9.3 Proposed verification process

1. The national programme manager prepares a detailed dossier describing the evidence for absence of transmission throughout the country.

2. The national programme manager may request assistance in preparing the dossier from WHO, the RPRG or WHO collaborating centres.

3. The national programme manager submits the dossier to the RPRG through the WHO regional office. The RPRG:

- reviews the proposal;
- may request that an expert team review the dossier and visit the country if necessary; and
- makes its recommendations on the basis of verification guidelines to the STAG-NTD M&E Working Group through WHO headquarters.

4. The STAG-NTD M&E Working Group reviews the recommendations of the RPRG and gives its recommendations to WHO STAG-NTD to either:

(a) accept the claim of the country regarding absence of transmission, resulting in its removal from the list of filariasis-endemic countries; or

(b) recommend further measures to be taken by the country to complete verification of absence of transmission.

References and other sources of information

10.1 References

1. Lymphatic filariasis. *Weekly Epidemiological Record*, 2001, 20:149–156.
2. *World Health Report 1995: bridging the gaps*. Geneva, World Health Organization, 1995.
3. *Preparing and implementing a national plan to eliminate lymphatic filariasis (in areas where onchocerciasis is not co-endemic)*. Geneva, World Health Organization, 2000 (WHO/CDS/CPE/CEE/2000.15).
4. *Preparing and implementing a national plan to eliminate lymphatic filariasis (in areas where onchocerciasis is co-endemic)*. Geneva, World Health Organization, 2000 (WHO/CDS/CPE/CEE/2000.16).
5. Horton J et al. An analysis of the safety of the single dose, two drug regimens used in programmes to eliminate lymphatic filariasis. In: Stephenson LS et al., eds. Controlling intestinal helminths while eliminating lymphatic filariasis. *Parasitology*, 2000, 121(Suppl.):S147–S160.
6. Report on the mid-term assessment of microfilaraemia reduction in sentinel sites of 13 countries of the Global Programme to Eliminate Lymphatic Filariasis. *Weekly Epidemiological Record*, 2004, 79:358–365.
7. Gyapong JO et al. Treatment strategies underpinning the global programme to eliminate lymphatic filariasis. *Expert Opinion on Pharmacotherapeutics*, 2005, 6:179–200.
8. Editorial Board of Control of Filariasis in China. *Control of lymphatic filariasis in China*. Manila, World Health Organization Western Pacific Region, 2003.
9. Stolk WA et al. Prospects for elimination of bancroftian filariasis by mass drug treatment in Pondicherry, India: a simulation study. *Journal of Infectious Diseases*, 2003, 188:1371–1381.
10. Michael E et al. Mathematical modeling and the control of lymphatic filariasis. *Lancet*, 2004, 4:223–234.

11. Global programme to eliminate lymphatic filariasis: progress report on mass drug administration in 2009. *Weekly Epidemiological Record*, 2010, 85:365–372.
12. *Preventive chemotherapy in human helminthiasis*. Geneva, World Health Organization, 2006.
13. Stephenson LS et al., eds. Controlling intestinal helminths while eliminating lymphatic filariasis. *Parasitology*, 2000, 121(Suppl.):S1–S173.
14. Massa K et al. The combined effect of the Lymphatic Filariasis Elimination Programme and the Schistosomiasis and Soil-transmitted Helminthiasis Control Programme on soil-transmitted helminthiasis in schoolchildren in Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2009, 103:25–30.
15. *Deworming school-aged children*, 2nd ed. Geneva, World Health Organization, 2011 [in press].
16. Boyd A et al. A community-based study of factors associated with continuing transmission of lymphatic filariasis in Leogane, Haiti. *PLoS Neglected Tropical Diseases*, 2010, 4(3):e640 (doi:10.1371/journal.pntd.0000640).
17. Kyelem D et al. Determinants of success in national programs to eliminate lymphatic filariasis: a perspective identifying essential elements and research needs. *American Journal of Tropical Medicine and Hygiene*, 2008, 79(4):480–484.
18. Swaminathan S et al. Mathematical models for lymphatic filariasis transmission and control: challenges and prospects. *Parasites & Vectors*, 2008, 1:2 (doi: 10.1186/1756-3305-1-2).
19. Tisch DJ et al. Mass chemotherapy options to control lymphatic filariasis: a systematic review. *Lancet Infectious Diseases*, 2005, 5:514–523.
20. Duerr H-P et al. Determinants of the eradicability of filarial infections: a conceptual approach. *Trends in Parasitology*, 2005, 21(2):88–96.
21. Burkot T, Ichimori K. The PacELF programme: will mass drug administration be enough? *Trends in Parasitology*, 2002, 18(3):109–115.
22. Lammie PJ et al. Unfulfilled potential: using diethylcarbamazine-fortified salt to eliminate lymphatic filariasis. *Bulletin of the World Health Organization*, 2007, 85:545–549.
23. *Global Programme to Eliminate Lymphatic Filariasis progress report 2000–2009 and strategic plan 2010–2020*. Geneva, World Health Organization, 2010 (WHO/HTM/NTD/PCT/2010.6).
24. Schuetz A et al. Evaluation of the whole blood filariasis ICT test for short-term monitoring after antifilarial treatment. *American Journal of Tropical Medicine and Hygiene*, 2000, 62(4):502–503.
25. Supali T et al. Detection of filarial-specific IgG4 antibodies using Brugia Rapid test in individuals from an area highly endemic for *Brugia timori*. *Acta Tropica*, 2004, 90:255–261.
26. *Operational guidelines for rapid mapping of bancroftian filariasis in Africa*. Geneva, World Health Organization, 2000 (WHO/CDS/CPE/CEE/2000.9).
27. Michael E et al. Mathematical models and lymphatic filariasis control: monitoring and evaluating interventions. *Trends in Parasitology*, 2006, 22(11):529–535.

28. Michael E et al. Mathematical models and lymphatic filariasis control: endpoints and optimal interventions. *Trends in Parasitology*, 2006, 22(5):226–33.
29. El-Setouhy M et al. The effect of compliance on the impact of mass drug administration for elimination of lymphatic filariasis in Egypt. *American Journal of Tropical Medicine and Hygiene*, 2007, 77(6):1069–1073.
30. Global programme to eliminate lymphatic filariasis: conclusions of the meeting of the Technical Advisory Group on the Global Elimination of Lymphatic Filariasis, November 2007. *Weekly Epidemiological Record*, 2008, 83: 341–347.
31. Babu BV, Mishra S. Mass drug administration under the programme to eliminate lymphatic filariasis in Orissa, India: a mixed-methods study to identify factors associated with compliance and non-compliance. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2008, 102:1207–1213.
32. *Monitoring drug coverage for preventive chemotherapy*. Geneva, World Health Organization, 2010 (WHO/HTM/NTD/PCT/2010.1).
33. *Working group on guidelines for stopping MDA and post-MDA surveillance for the elimination of lymphatic filariasis*. August 7–8, 2008 [unpublished report]. Geneva, World Health Organization.
34. Amarillo MLE et al. Factors associated with the acceptance of mass drug administration for the elimination of lymphatic filariasis in Agusan del Sur, Philippines. *Parasites & Vectors*, 2008, 1(14) (doi:10.1186/1756-3305-1-14).
35. Lahariya C, Mishra A. Strengthening of mass drug administration implementation is required to eliminate lymphatic filariasis from India: an evaluation study. *Journal of Vector Borne Diseases*, 2008, 45(4):313–320.
36. *Immunization coverage cluster survey - reference manual*. Geneva, World Health Organization 2005. (WHO/IVB/04.23/2005).
37. Mladonicky JM et al. Assessing transmission of lymphatic filariasis using parasitologic, serologic, and entomologic tools after mass drug administration in American Samoa. *American Journal of Tropical Medicine and International Health*, 2009, 89(5):769–773.
38. Grady C et al. Endpoints for lymphatic filariasis programs. *Emerging Infectious Diseases*, 2007, 13(4):608–610.
39. Weil GJ, Ramzy RMR. Diagnostic tools for filariasis elimination programs. *Trends in Parasitology*, 2006, 23(2):78–82.
40. Simonsen PE et al. Lymphatic filariasis control in Tanzania: Effect of repeated mass drug administration with ivermectin and albendazole on infection and transmission. *PLoS Neglected Tropical Diseases*, 2010, 4(6):e696 (doi: 10.1371/journal.pntd.0000696).
41. Tisch DJ et al. Mass drug administration trial to eliminate lymphatic filariasis in Papua New Guinea: changes in microfilaremia, filarial antigen, and Bm14 antibody after cessation. *American Journal of Tropical Medicine and Hygiene*, 2008, 78(2):289–293.
42. Baker MC et al. Mapping, monitoring, and surveillance of neglected tropical diseases: towards a policy framework. *Lancet*, 2010, 375:231–238.
43. Deming M, Lee H. *Filarial antigenemia surveys: a manual for survey planners* [draft document dated January 2011; available at: http://www.filariasis.us/resources.html].

44. Deming M, Lee H. Background and technical notes for *Filarial antigenemia surveys: a manual for survey planners* [draft document dated January 2011; available at: http://www.filariasis.us/resources.html].
45. Helmy H et al. Bancroftian filariasis: effect of repeated treatment with diethylcarbamazine and albendazole on microfilaraemia, antigenaemia and antifilarial antibodies. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2006, 100:656–662.
46. Jamail M et al. Field validation of sensitivity and specificity of rapid test for detection of Brugia malayi infection. *Tropical Medicine and International Health*, 2005, 10(1):99–104.
47. Joseph HM, Melrose W. Applicability of the filter paper technique for detection of antifilarial IgG4 antibodies using the Bm14 filariasis CELISA. *Journal of Parasitology Research*, 2010, doi:10.1155/2010/594687.
48. Cheun HI et al. Elimination of lymphatic filariasis in the Republic of Korea: an epidemiological survey of formerly endemic areas, 2002–2006. *Tropical Medicine and International Health*, 2009, 14(4):445–449.
49. Pedersen EM et al. The role of monitoring mosquito infection in the Global Programme to Eliminate Lymphatic Filariasis. *Trends in Parasitology*, 2009, 25(7):319–327.
50. Farid HA et al. A critical appraisal of molecular xenomonitoring as a tool for assessing progress toward elimination of lymphatic filariasis. *American Journal of Tropical Medicine and Hygiene*, 2007, 77(4):593–600.
51. Laney SJ et al. A reverse transcriptase-PCR assay for detecting filarial infective larvae in mosquitoes. *PLoS Neglected Tropical Diseases*, 2008, 2(6):e251 (doi:10.1371/journal.pntd.0000251).
52. Recommendations of the International Task Force for Disease Eradication. *Morbidity and Mortality Weekly Report*, 1993, 42 (RR-16):1–38.

10.2 Other sources of information

Guidelines for certifying lymphatic filariasis elimination (including discussion of critical issues and rationale). Geneva, World Health Organization, 1999 (WHO/FIL/99/197).

Report of a WHO informal consultation on epidemiologic approaches to lymphatic filariasis elimination: initial assessment, monitoring, and certification. Atlanta, 2–4 September, 1998. Geneva, World Health Organization, 1999 (WHO/FIL/99/195).

STAG-NTD M&E Sub-Working Group on Disease-Specific Indicators. *Meeting report: evaluation of the "stopping MDA" protocol and recommendations for post-MDA surveillance*. 14 July 2010 [unpublished report]. Atlanta, GA, USA.

Verification of absence of transmission for lymphatic filariasis elimination programs: criteria, strategies and procedures for different country situations [draft guidelines]. 8 April, 2004. Geneva, World Health Organization [LF-TAG, Monitoring and Evaluation Sub-Group].

World Health Organization Mission to China for the Preparation of Documentation for the Official Verification of Elimination of Lymphatic Filariasis 10–18 June, 2004 [unpublished report]. Manila, World Health Organization Western Pacific Region.

Annexes

Annex 1. Measuring the prevalence and density of microfilariae in sentinel and spot-check sites

The prevalence and density of microfilariae can also be used to measure the impact of MDA. The standard method of night-blood surveys of the sentinel site population aged >5 years is used to determine the prevalence and density of microfilariae.

The microfilaria prevalence (mf %) is calculated as the proportion of blood slides found positive for microfilariae, i.e.:

$$\frac{\text{no. of individuals whose slides are positive for microfilariae}}{\text{total no. of individuals examined for microfilariae}} \times 100$$

The microfilarial density (mfd) is the average number of microfilariae in slides found positive for microfilariae per ml of blood[1] (presuming 60 µl per slide) calculated as:

$$\frac{\text{total count of microfilariae in the slides found positive}}{\text{total no. of slides found positive}} \times 16.7$$

[1] *Bench aids for the diagnosis of filarial infections*. Geneva, World Health Organization, 1997.

Example: You have to tally the density of microfilariae in 10 samples. All the blood samples have been collected as a 60 µl sample (*Table A.1.1*).

Table A.1.1 Example showing tally of density of microfilariae in 10 blood films

Serial no. of person tested	No. of microfilariae
1	120
2	0
3	0
4	0
5	0
6	60
7	0
8	0
9	0
10	0
Total number of microfilariae	**180**

For this exercise, take an imaginary population of 10 people, rather than 500 as would be used in reality. Only two films are positive, giving a total of 180 microfilariae.

If we apply the formula:
180 × 16.7/2 = 1503 mf we find that in this site the mean density is 150 microfilariae/ml.

If a volume other than the recommended 60 µl is used for making blood slides, an appropriate multiplication factor other than 16.7 is needed to calculate the mfd.

Table A.1.2 can be used to obtain the multiplication factor.

Table A.1.2 Multiplication factors for different blood volumes

Volume of blood used	Multiplication factor
60µl	x 16.7
100µl	x 10

Recommended procedures for the detection and identification of microfilariae in blood

Microfilariae appear in the blood with a marked nocturnal periodicity in most situations. Some species and strains, however, are nocturnally subperiodic or diurnally subperiodic (*Table A.1.3*).

Table A.1.3 Characteristics of common human lymphatic filarial parasites

Characteristics	*B. malayi*	*B. timori*	*W. bancrofti*
Geographical distribution	South-east Asia, Indian subcontinent	Lesser Sunday Islands, Timor-Leste	Tropical and subtropical countries
Vectors	Mosquitoes (*Anopheles* and *Mansonia spp.*)	Mosquitoes (*Anopheles spp.*)	Mosquitoes (*Culex, Aedes, Anopheles* and *Mansonia spp.*)
Habitat			
Adults	Lymphatic system	Lymphatic system	Lymphatic system
Microfilariae	Blood	Blood	Blood
Periodicity of microfilariae	Nocturnal[a]	Nocturnal	Nocturnal[b]
Morphology of microfilariae			
Sheath	Present	Present	Present
Length (μm)	175–230 in films; 240–300 in 2% formalin	265–325 in films; 330–385 in 2% formalin	240–300 in films; 275–320 in 2% formalin
Width (μm)	5.0–6.0	4.4–6.8	7.5–10.0
Tail	Tapered; subterminal and terminal nuclei widely separated	Tapered; subterminal and terminal nuclei widely separated	Tapered; anucleate
Key features	Long head space, sheath stains pink in Giemsa; terminal and subterminal nuclei	Long head space; sheath unstained in Giemsa; terminal and subterminal nuclei	Short head space; sheath unstained in Giemsa; body in smooth curves; dispersed nuclei

[a] Nocturnally subperiodic in Indonesia, Malaysia, and parts of the Philippines and Thailand.
[b] Diurnally subperiodic in New Caledonia and Polynesia; nocturnally subperiodic in rural areas of Thailand.

The times for collection of blood specimens should be selected in accordance with the patient's clinical symptoms. *Table A.1.4* shows the recommended times for collecting blood specimens for testing for periodic and subperiodic species of microfilariae.

Table A.1.4 Recommended times for collection of blood specimens for testing for microfilariae

Species[a]	Recommended collection time
Periodic (nocturnal)	22:00–01:00 (peak 24:00)
Periodic (diurnal)	12:00–14:00 (peak 13:00)
Subperiodic (nocturnal)	20:00–22:00 (peak 21:00)
Subperiodic (diurnal)	15:00–17:00 (peak 16:00)
Aperiodic	Any time (day or night)

Preparation of blood film for examining microfilariae

1. Clean slide with an alcohol swab to remove lint and oil residue.

2. Label the slide.

3. With the patient's left hand palm upwards, select the third or fourth finger. (The big toe can be used with infants. The thumb should never be used for adults or children.) Use cotton wool lightly soaked in ethanol to clean the finger – using firm strokes to remove dirt and grease from the ball of the finger (*Figure A.1.1*). Dry the finger with a clean piece of cotton wool (or lint).

Figure A.1.1 Cleaning the finger before collecting a capillary blood sample

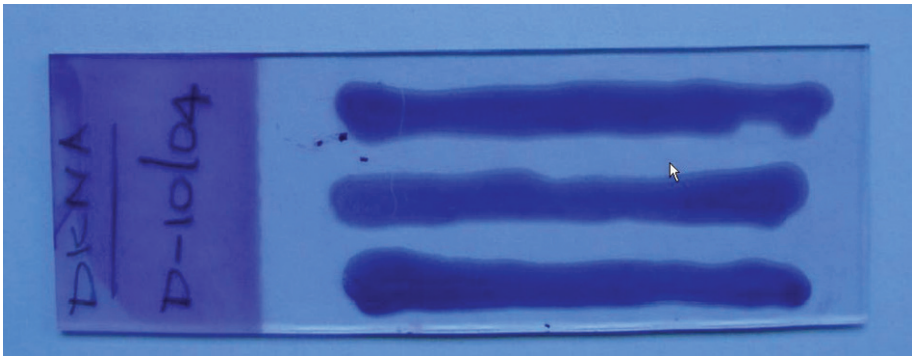
4. With a sterile lancet, puncture the internal side of the finger (*Fig. A.1.2*) using a quick rolling action. By applying gentle pressure to the finger, express the first drop of blood and wipe it away with dry cotton wool. Make sure that no strands of cotton wool remain on the finger. Discard the lancet into a sharp's container.

Figure A.1.2 Using a lancet to puncture the tip of the finger

5. Working quickly and handling clean slides only by the edges, collect the blood as follows:

   - Apply gentle pressure to the finger and collect 60 µl of blood into a blood collection tube or calibrated capillary tube.
   - It helps to hold the capillary tube horizontal (flat) as you collect the blood.
   - Try not to get air bubbles into the capillary tube. If you do, fill the blood past the line to compensate.
   - Wipe the remaining blood away with cotton wool. Ask the patient to hold the cotton wool firmly on the finger until it stops bleeding.

Figure A.1.3 Preparing a blood film



6. Always handle slides by the edges, or by a corner, to make the film as follows:

    - Using the micropipettor or capillary tube prepare three parallel lines of blood (20µl each) along the length of the slide (*Fig. A.1.3*).
    - Air dry the blood film thoroughly for 24–72 hours. Carefully, load the slides into the staining racks.
    - Dehaemoglobinize the blood film for approximately 5 minutes in tap water, distilled water or normal saline.

Note: Dehaemoglobinization is necessary to clear the red blood cells so that the microfilariae can be more easily visualized, and is complete when the smear turns an opaque greyish-white. Caution must be exercised at this time because the smear is fragile, and rough washing or agitation can result in its floating off the slide. Although fixation in methanol is not absolutely necessary, it results in better staining of the microfilariae.

- Air dry. This can be done in the staining racks.
- Fix in methanol 3–5 minutes.
- Stain with Giemsa.

Note: With Giemsa staining, the general rule is to stain for the length of time equivalent to the concentration of the stain. Routinely we use a 1:50 dilution of stock Giemsa and stain for 50 minutes. As a rule of thumb, if the white blood cell nuclei are properly stained, microfilariae should also be adequately stained. It should be noted that for Giemsa staining of films to be examined for microfilariae, unlike those to be examined for malaria parasites, the pH of the staining solution is not critical. The overall colour of the film may range from pink to purple to blue, depending on the pH, but the microfilariae will be stained adequately regardless of colour.

- Air dry.

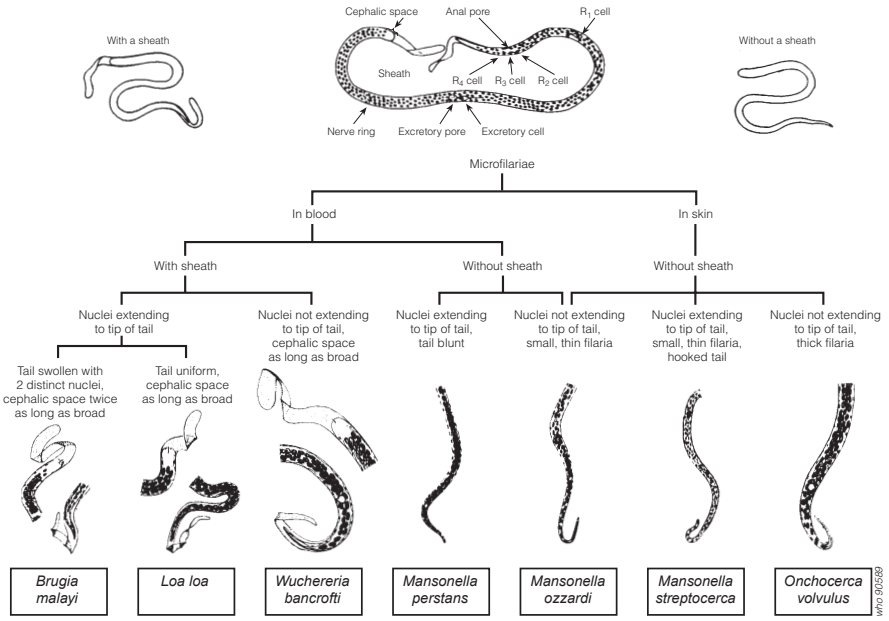
7. Examine the preparation under the microscope. Use the x 10 objective first to locate the microfilariae; then identify the filarial species using the x 40 and x 100 objectives.

Results

Under the light microscope, microfilariae appear (after appropriate staining) as primitive organisms, serpentine in shape, often enclosed in a sheath and filled with the nuclei of many cells (*Fig. A.1.4*).

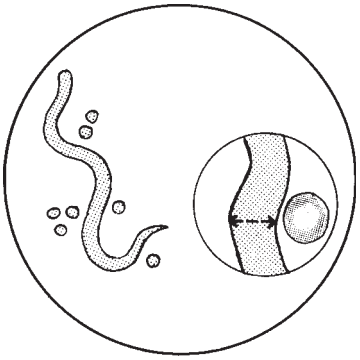
Not all species have a sheath. In those that do, the sheath may extend a short or long distance beyond either extremity. In some species, depending on the stain used, the sheath displays a unique staining quality which aids in species identification.

Figure A.1.4 Microfilariae found in humans R1, R2, R3, R4: rectal cells



The nuclei of the cells that fill the body are usually darkly stained and may be crowded together or dispersed (*see Fig. A.1.4*). The anterior extremity is characteristically devoid of nuclei and is called the cephalic or head space; it may be short or long.

Figure A.1.5 Length of pathogenic microfilaria: 250–300 µm; thickness 6–8 µm (diameter of an erythrocyte), e.g. *W. bancrofti*, *Loa Loa*, *Brugia spp*.



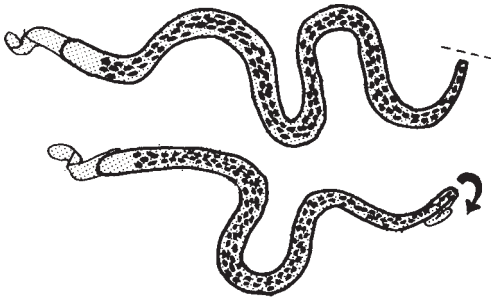
As you look from the anterior to the posterior end of the body you will see additional spaces and cells that serve as anatomical landmarks. These include the nerve ring, excretory pore, excretory cell and anal pore. In some species an amorphous mass called the inner body and four small cells (known as rectal cells) can be seen. Some of these structures and their positions are useful in identifying the species. Other useful features include the shape of the tail and the presence or absence of nuclei within it.

Note: Sometimes the microfilariae of the periodic strain of *B. malayi* lose their sheath. Identification of species can be difficult and mistakes are frequently made. The guidelines for the identification of microfilariae given above and those that appear in most textbooks make identification seem deceptively simple. Sometimes it is difficult to see the sheath. At other times, the nuclei do not appear in their characteristic position at the tip of the tail. It is good practice to examine several microfilariae carefully, before deciding on their species. If a systematic study is made of all the characteristics mentioned above, it should be possible to identify with certainty the species observed. The identification must not be based on a single characteristic, but on all the features taken together.

Possible causes of misidentification

- ***Broken or folded tail***. If the tail of *W. bancrofti* is broken or folded over (*Fig. A.1.6*), it appears to have nuclei extending to the tip as with *Loa loa*.
- ***Torn or colourless sheath***. The sheath is sometimes torn or almost colourless. In *Loa loa*, for example, the sheath appears as a colourless space between the tail and the blood cells.
- ***Unusually large or small microfilariae***. Some *Mansonella* perstans are very long (e.g. 200 µm), and some *W. bancrofti* and *Loa loa* are small (e.g. 250 µm).
- ***Badly made smears (or films)***. If it is damaged when the smear (or film) is being made, *W. bancrofti* may appear twisted and *Loa loa* may show a few curves.
- ***Examination of thin films***. Identification of microfilariae in stained thin films is not recommended; the microfilariae are shrunken, distorted and difficult to recognize.

Figure A.1.6 Possible cause of misidentification of *W. bancrofti*: broken or folded tail



Annex 2. Immunochromatographic test protocol

The ICT card test has been shown to be useful and sensitive tool for the detection of *Wuchereria bancrofti* antigen and is being used widely by lymphatic filariasis elimination programmes. Although the test is relatively simple to use, adequate training is necessary to reduce inter-observer variability and to reduce the misreading of cards which can lead to false positive results.

Basic guidelines

i. Cards are currently known to have a limited shelf life at ambient temperatures (3 months at 30°C) but longer shelf life when stored at 4°C (approximately 9 months). Cards should NOT be frozen.

ii. One hundred microliters of blood should be collected by finger prick into a calibrated capillary tube coated with an anticoagulant (EDTA or heparin). Alternatively, finger prick blood can be collected into a microcentrifuge blood collection tube coated with either EDTA or heparin.

iii. Before beginning field surveys, two cards from each lot of cards should be tested using a weak positive control that can be obtained from the Filariasis Research Reagent Repository Center (*www.filariasiscenter.org*). When using this control, the test line can be very faint. DO NOT use cards that are negative when tested with the control.

iv. When transporting cards for use in the field, a cool box is not required. However, care should be taken not to expose cards to extreme heat for prolonged periods of time.

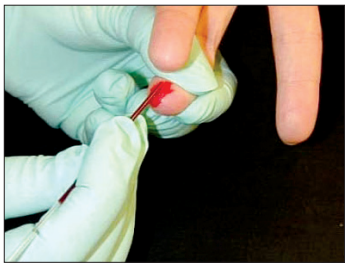
v. Cards must be read using adequate lighting. Faint lines can be difficult to see when lighting is not adequate. This is especially important when reading cards at night.

Test procedures

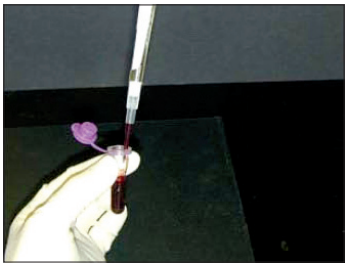
1

Remove cards from pouch just prior to use.

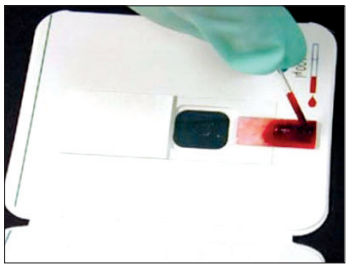
2



Collect 100 µl blood finger prick using a calibrated capillary tube OR measure 100 µl of blood from a microcentrifuge tube using a micropipettor. DO NOT add blood directly from the finger to the card.



3



Add blood sample slowly to the white portion of the sample pad.

DO NOT add blood directly to the pink portion of the sample pad.

DO NOT close the card before the sample migrates to the pink portion of the sample pad (take approximately 30 seconds after adding blood).

Annex 3. Brugia Rapid™ test protocol

The Brugia Rapid™ test is an immunochromatographic (lateral flow) antibody assay in the cassette format. It uses *Brugia malayi* recombinant protein (B*m*R1) and detects specific human IgG4 to *B. malayi* and *B. timori*. The assay takes about 25 minutes using whole blood samples and 15 minutes using serum or plasma samples.

Basic guidelines

i. The test is known to have a shelf life of 18 months when stored at ambient temperatures (20–25°C); however, for long-term storage, 4°C (refrigeration) is recommended. The tests should NOT be frozen.

ii. Each cassette is packed in individually sealed aluminum pouch. Open the pouch just prior to use.

iii. When transporting tests for use in the field, a cool box is not required, although desirable. However, care should be taken not to expose the tests to extreme heat for prolonged periods of time.

iv. Tests must be read using adequate lighting. Faint lines can be difficult to see when lighting is not adequate. This is especially important when reading tests at night.

v. The test uses 25 µl serum or plasma or 35 µl whole blood.

Sample collection

For testing of whole blood sample, 35 µl of whole blood from the pricked finger needs to be collected and placed into the square well of the test cassette (refer to Step 1 in the Assay Procedure). There are three methods to do this step, namely:

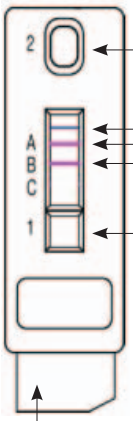
a. The 35 µl whole blood can be collected from the finger using a calibrated microcapillary tube with anti-coagulant and added to the square well of the test cassette (procedure for preparing the calibrated microcapillary tube is given in the product insert).

b. Several drops of blood from the finger can be collected directly into a micro collection tube coated with anti-coagulant. Before performing the test, 35 µl of blood can be taken up using a micropipettor.

c. The 35 µl whole blood can be directly pipetted from the finger and immediately delivered into the square well, making sure that there is no air bubble. However this method should only be performed by an experienced person to avoid pipetting the incorrect volume of blood.

Test procedure

1. Bring test cassette and chase buffer to room temperature (if precipitate is noted in the chase buffer, shake the bottle vigorously and allow it to warm up further).
2. Open the pouch by gently tearing at the notch of the pouch.
3. Label the test device with the sample name.
4. Proceed with the assay procedure as diagrammed below.



Step 2: Add 3 drops of chase buffer; drop-by-drop and let it sip through the pad in between the drops. Go to step 3.

Blue line
A = control line
B = test line

Step 1:
For serum or plasma samples:
Add 25 µl of sample to square well.

For whole blood samples:
Add 35 µl of sample to square well followed by 1 drop of chase buffer to the same well.
Serum/plasma will start wicking up the membrane. Red blood cells will wick slower. The cassette may be tapped gently on the table to facilitate the sample to flow up the membrane. Wait until the wet sample front of the serum/plasma reaches the blue line. Go to step 2. In the rare event that the sample front does not reach the blue line after waiting for approximately 3 minutes, please proceed to step 2.

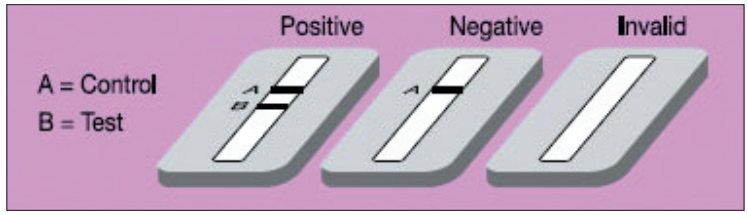
Step 3: Pull clear tab until resistance is felt. Add 1 drop of chase buffer to the square well. Start timing. Read results within 15 minutes for serum/plasma and within 25 minute for whole blood.

Interpretation of results

Any intensity of band (line) at B should be considered as positive

1. **Positive** for either *B. malayi* and/or *B. timori* specific antibodies if coloured bands appear at the Control line (A) and Test line (B) as shown in the diagram above.
2. **Negative** for *B. malayi* and *B. timori* specific antibodies if only the Control line (A) is visible through the viewing window.

Invalid if the Control line (A) is absent. If this occurs, the assay should be repeated using a new test cassette.



Annex 4. Cluster-survey protocol for assessing coverage of mass drug administration

Introduction

This protocol is designed to assist LF programme managers in implementing population-based cluster surveys of coverage to complement the "reported coverage" obtained from tally sheet data[1].

Representative surveys provide a method for confirming results for reported coverage, and are especially important if there is doubt about the reported data. Additional information can economically be collected during the coverage survey by adding questions related to topics such as knowledge about LF, side-effects experienced and other aspects of the Programme.

This protocol provides a standardized sampling methodology, modelled on immunization coverage surveys, which is designed to strike a balance between statistical rigour and practical implementation. The sampling methodology is designed to provide an estimate of actual coverage accurate to within plus or minus 6.5%.

This protocol involves a series of steps, including:

- selection of the IU to be surveyed;
- selection of subunits or areas (e.g. villages, wards or localities) within the IU, using population-proportionate sampling to weigh these areas according to their population size;
- random selection of a starting household followed by sampling from a cluster of contiguous households; and
- use of a simple tabular data form and questionnaire to determine whether household members participated in the MDA.

Various forms and instructions useful in carrying out a cluster survey are included:

- A draft template questionnaire
- A random number table
- An example of population-proportionate sampling
- Details on selection of a starting household
- A table with examples of sample sizes for use under different assumptions and conditions

[1] Alternative methods, such as LQAS, have been proposed for small geographical areas where random selection of individuals is possible. LQAS may provide a means to identify areas that fail to meet a defined coverage criterion. This method is not covered in this protocol.

Purpose

The purpose of a population-based survey is to provide a coverage estimate that is statistically likely to be representative of the population sampled. The estimate does not depend on data aggregated from different distribution sites, and thus is not as subject to missing data, mathematical errors or difficulties with estimating an accurate denominator from census figures.

Sampling

Ideally, to get a representative response from individuals living in a given IU (usually a district) or a cluster of IUs, all individuals should be listed, and a sample of these individuals selected at random. Because this is impractical, the best compromise is to ensure random selection of smaller areas within the survey area, and to select individuals randomly from within these smaller areas. In order to do this, a smaller geographical area needs to be defined – this is usually an enumeration unit, a village, ward, locality or other administrative division of the district. To simplify analysis, the selection of these smaller units is made in proportion to the size of the population.

Once the smaller subunits have been selected, it is important to ensure that every individual within the subunit has an equal likelihood of being selected for the survey. Various methods are used to achieve this. The simplest is to randomly select a "starting household", interview all its members and then select contiguous households until the desired number of individuals has been interviewed.[1] For some subunits, it will be necessary to make further subdivisions using random selection techniques until the number of households in the subunit is small enough to be easily enumerated. Once the household has been selected, everyone in that household is interviewed.

Interpretation

This survey technique provides a representative estimate of the population coverage rate. The accuracy of this estimate depends on several factors, including the number of people included in the sample, the potential error introduced by sampling people together within a subunit rather than as randomly selected individuals – the so-called design effect – and the true population coverage rate. The sample will be least accurate when the rate is 50%.

Table A.4.1 indicates how the interactions between sample size, design effect and true coverage rate affect the accuracy of the sample estimate. In the method described here, 30 people are selected from each of the 30 subunits giving a total sample size of 900. For an assumed design effect of 4, which in most cases is probably an overestimate, and a true coverage rate of 50% – in most cases probably an underestimate – the survey result will be within 6.5% of the true coverage figure 95% of the time. The estimate from the 30 subunits applies as an average for the entire area included in the sample. The results from a single subunit are not a valid estimate of that subunit.

[1] In the WHO Expanded Programme on Immunization, it is the "nearest to the left when leaving the house"; other criteria are used when in urban apartments on multiple floors. The issue is only to have a strict rule for selecting successive households.

Table A.4.1 Sample sizes for different anticipated coverage and design effects

Coverage	Precision	Design effect	Sample size	No. of people/clusters
50%	0.05	1	384	13
-	-	2	768	26
-	-	3	1152	38
-	-	4	1537	51
-	-	-	-	-
-	0.1	1	96	3
-	-	2	192	6
-	-	3	288	10
-	-	4	384	13
-	-	-	-	-
60%	0.05	-	369	12
-	-	-	738	25
-	-	-	1106	37
-	-	-	1475	49
-	-	-	-	-
-	0.1	-	92	3
-	-	-	184	6
-	-	-	277	9
-	-	-	369	12
-	-	-	-	-
70%	0.05	-	323	11
-	-	-	645	22
-	-	-	968	32
-	-	-	1291	43
-	-	-	-	-
-	0.1	-	81	3
-	-	-	161	5
-	-	-	242	8
-	-	-	323	11
-	-	-	-	-
50%	0.065	4	900	30
60%	0.06	4	-	-
70%	0.06	4	-	-

Methods

Selection of implementation units

The survey is done at the level of the IU, which is commonly a district. The IU, or aggregation of IUs to be surveyed, can be purposively selected, perhaps selecting those with high or low coverage, in order to include IUs where the programme is going well and those in which there may be difficulties.

The coverage estimate is representative of the IU being surveyed. A simple average of all IUs surveyed does not provide a statistically valid estimate of national coverage. Although such an estimate may hold some attraction politically, it does not identify IUs that are performing well or poorly. Although it is possible to sample individual IUs and combine results to give a national estimate, this increases costs and complexity, and should only be undertaken with expert statistical advice.

Selection of areas from which clusters of individuals will be sampled

For this protocol, within the selected survey area, 30 subunits need to be selected. From each of these, a cluster of individuals will be selected. The ideal subunit is an administrative unit for which population figures are available. The subunit may be a village, a statistical enumeration area (used for census determination), a ward or a locality.

These 30 subunits must be selected randomly from all subunits within the survey area. In addition, because different areas will have different populations, the areas need to be weighted to take these population differences into consideration. If weighting is done during selection, it is not necessary to weight the results during the analysis.

Stepwise directions for population-proportionate sampling are given in *Box A.4.1*. For this method of sampling, the following information is required:

There must be a clear definition of the subunit (e.g. village, ward, locality) within the survey area, and the ability to define its geographical boundaries when collecting field data.

A complete listing of all the subunits within the survey area is needed, taking care to ensure that no populated areas are excluded. If there is no listing, for example of villages for a given survey area, an alternative administrative unit may need to be chosen as the subunit, such as a ward. Estimated population figures for each subunit must be obtained.

Training programmes for survey workers should emphasize the importance of adhering to the principles of random selection with known probabilities. Once a subunit or starting household has been selected, it should be included in the sample. Substitutions invalidate random selection and easily lead to erroneous results.

Box A.4.1 Stepwise directions for population-proportionate sampling

Step 1. List all subunits within the area or IU to be surveyed. Within the selected area, make a complete list of all the subunits from which the cluster of individuals will be selected. The list does not need to be in any particular order, but must include all the subunits within the IU.

Step 2. List the population for each subunit. In a column next to the name of the subunit, list its estimated population. The source of the population figures is not critical as long as the same source is used for each area. Usually census figures (with appropriate correction if the census is old) are used.

Step 3. Calculate the cumulative population for the list of subunits. In a third column, successively add the population for each subunit, providing a cumulative population figure for the whole survey area. This can be done using a computer spreadsheet.

Step 4. Calculate the sampling interval. To calculate the sampling interval, divide the total population for the IU by 30 (the total number of subunits to be selected).

Step 5. Randomly select the starting point. Using a table of random numbers (see *Table A.4.2*), select a number between 1 and the sampling interval, and record this in a fourth column.

Step 6. Calculate populations from which to select the subsequent subunit. Add the sampling interval to the starting point, and record in the fourth column. Continue to add the sampling interval successively until the total population for the area is reached or exceeded.

Step 7. Select remaining subunits. Using the figures in the fourth column, determine if a subunit is to be included in the survey as follows. If the first random number (between 1 and the sampling interval) recorded in the fourth column includes the population of the first subunit listed (in the third column), then that subunit is selected as the first of the 30 areas to be selected. If the random number is larger, then the first subunit in which the cumulative population includes this random number is selected as the first subunit.

Using the next number in the fourth column, determine the next subunit that is included in that number, and continue making selections until all 30 subunits are selected. In some instances, an area will have a large population, and it is possible that it will be selected more than once.

See *Table A.4.3* for an example.

Table A.4.2 Table of random numbers

	1	2	3	4	5	6	7	8	9
1	10480	15011	1536	2011	81647	91646	69179	14194	62590
2	22368	46573	25595	85393	30995	89198	27982	53402	93965
3	24130	48390	22527	97265	76393	64809	15179	24830	49340
4	42167	93093	6243	61680	7856	16376	39440	53537	71341
5	37570	39975	81837	16656	6121	91782	60468	81305	49684
6	77921	6907	11008	42751	27756	53498	18602	70659	90655
7	99562	72905	56420	69994	98872	31016	71194	18738	44013
8	96301	91977	5463	7972	18876	20922	94595	56869	69014
9	89579	14342	63661	10281	17453	18103	57740	84378	25331
10	85475	36857	53342	53988	53060	59533	38867	62300	8158
11	28918	69578	88231	33276	70997	79936	56865	5859	90106
12	63553	40961	48235	3427	49626	69445	18663	72695	52180
13	9429	93969	52636	92737	88974	33488	36320	17617	30015
14	10365	61129	87529	85689	48237	52267	67689	93394	1511
15	7119	97336	71048	8178	77233	13916	47564	81056	97735
16	51085	12765	51821	51259	77452	16308	60756	92144	49442
17	2368	21382	52404	60268	89368	19885	55322	44819	1188
18	1011	54092	33362	94904	31273	4146	18594	29852	71685
19	52162	53916	46369	58586	23216	14513	83149	98736	23495
20	7056	97628	33787	9998	42698	6691	76988	13602	51851
21	48663	91245	85828	14346	9172	30163	90229	4734	59193
22	54164	58492	22421	74103	47070	25306	76468	26384	58151
23	32639	32363	5597	24200	13363	38005	94342	28728	35806
24	29334	27001	87637	87308	58731	256	45834	15398	46557
25	2488	33062	28834	7351	19731	92420	60952	61280	50001

Table A.4.3 Example of population-proportionate sampling

Subunit (e.g. village, ward)	Population	Cumulative population	Areas selected	Random start plus sampling interval	Sampling interval calculations
1	480	480			*Total population = 37741*
2	555	1035	1	718	*Total number of areas = 30*
3	657	1692			
4	489	2181	1	1976	
5	367	2548			
6	456	3004			
7	1299	4303	1	3234	*Sampling interval = 1258 (37741/30)*
8	345	4648	1	4492	
9	333	4981			
10	777	5758	1	5750	
11	888	6646			*Random start = random number between 1 and 1258*
12	675	7321	1	7008	
13	324	7645			
14	865	8510	1	8266	
15	567	9077			
16	756	9833	1	9524	*For this example, 718 was the randomly selected starting point*
17	1234	11067	1	10782	
18	3465	14532	2	12040	
				13298	
19	567	15099	1	14556	
20	878	15977	1	15814	
21	898	16875			
22	909	17784	1	17072	
23	345	18129			
24	345	18474	1	18330	
25	556	19030			
26	675	19705	1	19588	
27	564	20269			
28	867	21136	1	20846	
29	933	22069			
30	967	23036	1	22104	

.../...

.../...

Subunit (e.g. village, ward)	Population	Cumulative population	Areas selected	Random start plus sampling interval	Sampling interval calculations
31	876	23912	1	23362	
32	347	24259			
33	879	25138	1	24620	
34	1266	26404	1	25878	
35	1244	27648	1	27136	
36	2134	29782	2	28394 29652	
37	467	30249			
38	234	30483			
39	266	30749			
40	188	30937	1	30910	
41	399	31336			
42	789	32125			
43	987	33112	1	32168	
44	867	33979	1	33426	
45	856	34835	1	34684	
46	745	35580			
47	679	36259	1	35942	
48	346	36605			
49	457	37062			
50	679	37741	1	37200	
			30		

Selection of households within an area or subunit

Once the 30 subunits for the survey area have been identified, enumerators will need to sample a cluster of individuals from each of those areas. For this purpose, 30 individuals will be selected from each subunit, resulting in an overall sample size for the survey of 900 individuals.

In making the selection, all individuals must have an equal chance of being included in the survey. In practical terms, this is usually done by using methods to randomly selecting a "starting household". Only households that are occupied (currently serving as a residence, even though the inhabitants may be away) are considered in the sampling.

Ideally, households should be selected at random from a list of all households in the subunit. However, this is usually not possible, because such a list is seldom available. An alternative is to map all the households within the subunit, and maps permitting numbering of individual households may be available from other programmes (e.g. polio eradication). It is costly, however, to create maps for the survey, and for LF coverage surveys, alternative methods are recommended if maps are not already available. If the subunit selected is so large that it is difficult to identify a starting household, it should be further divided. First divide the subunit into manageable areas with approximately the same number of households and select one of these at random. Then select the starting household within that area.

The most important consideration is to have a practical mechanism that allows a starting household to be selected at random, with all households in the area having an equal chance of being selected.

In order of preference, the following selection methods are recommended:

1) Randomly select a starting household from a list of all households in the subunit.
2) Use a map to enumerate all households in the subunit and randomly select one. The map should ideally be updated in collaboration with a resident of the area who knows about recent changes.
3) Divide the subunit into quadrants with approximately the same number of households in each. Select one quadrant at random, list the households and select one of these households at random. If the quadrant is still too large, repeat the process dividing it again into a smaller number of areas.
4) From the approximate centre of the subunit, randomly select a direction of travel. Count the number of households between the centre and the limit of the subunit and randomly select the starting household.

More specific details on the methods for random selection of the starting household are given in *Box A.4.2*.

Box A.4.2 Random selection of the starting household

Randomly select a starting household from a list of all households in the subunit.

In this ideal but unlikely situation, randomly select one household from the full list by selecting a random number between 1 and the total number of households listed. This defines the "starting household". Beginning with this household, sample consecutive households as described in the text.

Randomly select a starting household from a map of all households in the subunit. The map should ideally be updated in collaboration with a resident of the area who knows about recent changes.

Maps may be available from recent demographic health surveys, national immunization days or census activities. Such a map can be used to number all households and list them. From this listing, it is possible to randomly select one household to serve as the starting household. Because consecutive households are sampled from this starting household, it will not matter if a few households are not on the list. However, if the map is grossly inaccurate, it should not be used.

Divide the subunit into smaller units such as quadrants, and following random selection of one of these, prepare a list of households within the smaller unit and randomly select the starting household.

Step 1. Identify a central point within the subunit through consultation with a village leader.

Step 2. Visually divide the subunit into a smaller number of units (such as quadrants), each with roughly the same number of households.

Step 3. Randomly select one of these smaller units for household sampling.

Step 4. Number all the households in the selected smaller unit and, by selecting a random number between 1 and the total number of households, select the starting household. If the smaller unit or quadrant proves to be too large to allow all households to be numbered, it can be divided again into smaller areas each with roughly the same number of households, repeating the process until a starting household can be randomly selected.

Randomly select a direction of travel, and after counting all households in that direction of travel, randomly select a starting household.

Step 1. Identify a central point within the subunit through consultation with a village leader.

Step 2. Spin a pen or bottle to randomly select a direction of travel from the central point. If there are no households in that direction, change the direction clockwise until the first house is encountered. This becomes the new direction.

Step 3. Number all households that fall along the line of travel in this direction starting from the central point and finishing at the boundary of the area or subunit. It is important to stick as closely as possible to the actual line of the direction of travel.

Step 4. Randomly select a number between 1 and the total number of households encountered along the direction of travel, and use this as the starting household.

Selection of individuals within the area or subunit

Once the starting household has been selected, data are collected from all individuals in that household. Once this has been done, the next nearest household is selected, and data are collected from all individuals in that household. This process continues until data have been collected from 30 individuals. If there are more individuals in the last household visited than are needed to reach the required total of 30, data on all individuals in the final household are collected, resulting in a sample of more than 30 for that particular cluster.

After completing the survey in the starting household, to select the next household, choose the one whose entrance is nearest to the starting household. Continue selecting additional households in this manner (excluding those already visited) until enough households have been visited to allow 30 individuals to have been sampled.

There are a number of definitions and criteria that apply to selection of individuals within households. The following general guidelines should be followed:

- All individuals who were living in the household during the time of the last MDA are enumerated. The list includes individuals who may not have been eligible (e.g. pregnant women), and those who may not currently reside in the household, or those not currently present. From this list, responses are tabulated.
- Ideally, each individual should answer for him or herself. Parents or caregivers can answer for young children. If a resident of the household is absent, a family member can provide information for that person if the enumerator judges that the response given by the family member is likely to be accurate.
- The questions include whether the person was treated with antifilarial drugs or not, and if not, whether it was because they were not eligible. For those who were not eligible, the reason for ineligibility is recorded (e.g. age, pregnancy or illness). For those who were eligible but did not receive the dose, the reason for not having received the dose is recorded (including refusal, not knowing about the MDA, or because of other obstacles such as knowing about MDA but being in the fields, travelling or away at work).
- Individuals enumerated, but on whom no information is available, are noted, but not included in the overall sample.
- The optional questions are asked of one respondent per household.
- The total sample should include 900 individuals on whom information is available.

The coverage survey is designed to capture data on a sample of 30 individuals for each area or subunit, rather than on a sample of a fixed number of households within each area. Thus, the total number of households visited will depend on the number of people in the households – if the average number of occupants is high, fewer households will be visited.

Analysis

Currently, the recommendation for reporting epidemiological drug coverage is to report the total number of individuals dosed divided by the total population of the endemic areas. For coverage surveys, therefore, the coverage estimate is based on the total number of individuals who state that they were dosed during the last MDA divided by all those on whom information is available who were resident in the households sampled at the time of the last MDA.

The basic analysis for the coverage survey is simple, and can be done by hand. Data collected using the template for a data collection form in the Appendix to this Annex can be used to produce a table with basic information on each of the 30 individuals sampled from each area, and a summary table for all areas can easily be created. In this way it is possible to determine the total number of people surveyed and the total number who stated that they received a dose during the recent MDA.

In the analysis, the numerator used for coverage is the total number of people who responded that they had received the dose during the recent MDA, and the denominator is the total number of people for whom data were available; both those who did and did not receive the dose. In addition, it will be useful to report in the analysis:

- the proportion of the total sample on whom no data were available;
- the proportion of the sample on whom information was available who were deemed ineligible, and the reasons for ineligibility;
- the proportion of the sample on whom information was available who were eligible and who refused dosing; and
- the proportion of the sample on whom information was available and who were eligible for dosing, but who did not receive the dose because they were not aware of the MDA.

With this sampling method, it is not statistically valid to define coverage for any given area or subunit from which the cluster of individuals has been selected — or to compare coverage between these areas. However, it may be possible to look at coverage for different domains within the overall sample of 900 individuals to see if there are gross differences for example, between men and women, or between adults and children.

Interpretation should be done with caution, however, because the smaller sample size for these strata makes the confidence interval wider, making it more difficult to determine statistically valid differences between strata.

It may be useful to enter the data into a spreadsheet or database to make sub-analyses easier, and to manage numerous coverage surveys over time. If additional questions are asked of individuals within households, for example about their knowledge, awareness, behaviour or practice, computerized records will be necessary, and this information may be valuable to review over time.

Appendix

Date dd/mm/yy Name of interviewer_____
Subunit _____ |__|__| Household no. _____

Part I: Template for questionnaire

NAME	SEX	AGE	DID EACH MEMBER OF THE HOUSEHOLD TAKE THE DRUGS?						ABSENT/ NO DATA
			Yes	No	Not eligible	Reason why not eligible? A = age/weight P = pregnant I = serious illness or hypersensitivity	Eligible but did not take dose	Reason for not taking dose: R = refused H = did not hear about MDA W = away at work, travelling	
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									

Part II: Optional questions to ask of one key respondent from each household

1) How did you know about the MDA (tick all unprompted responses)?

- ☐ Heard from friend or neighbour
- ☐ Heard about it on the radio
- ☐ Heard about it on the television
- ☐ Saw poster or pamphlet
- ☐ Heard about it from a health worker

2) What can you tell me about lymphatic filariasis (tick all unprompted responses)?

- ☐ Transmitted by mosquitoes
- ☐ Causes "bigfoot"
- ☐ Causes hydrocele
- ☐ Can be prevented

3) Are there any members of this household with hydrocele (use local terms where possible)?

- ☐ Yes
- ☐ No

4) If yes, have they received treatment for this condition?

- ☐ Yes
- ☐ No

Describe treatment: _____
_____

5) Are there any members of this household with lymphoedema (use local term where possible)?

- ☐ Yes
- ☐ No

6) If yes, have they received treatment for this condition?

- ☐ Yes
- ☐ No

Describe treatment:_____
_____

7) (For those who participated in the MDA) Why did you participate in the recent MDA?

- ☐ Told to by a health worker, radio or television spot
- ☐ Concerned about the disease
- ☐ Worried about transmission
- ☐ Wanted to prevent transmission to future children

8) What did you like about the MDA?

- ☐ Easy to get to distribution site
- ☐ House-to-house distribution (if applicable)
- ☐ Knowledgeable distributors
- ☐ No long wait for drugs
- ☐ Received other information or services

9) What didn't you like about the MDA?

- ☐ Site too far away
- ☐ Drugs ran out or were not available
- ☐ Unfriendly distributor
- ☐ Took too much time
- ☐ Did not dose other members of my family
- ☐ Adverse reactions to drugs

Annex 5. Detailed protocol for Transmission Assessment Survey

Given the time needed to collect preliminary data, formulate the survey design, inform selected survey schools and/or communities, prepare logistics and organize field teams, it is highly recommended that the following tasks be completed several weeks in advance of the survey start date.

Selecting sites and individuals for inclusion in survey

Randomized site selection

A numbered list of all primary schools (for school-based surveys) or EAs (for community-based surveys) in the EU should be prepared in advance by the country programme manager. To achieve a better geographical distribution of the EU, the school or EA list should be numbered by geographical proximity as opposed to alphabetical order. *The Survey sample builder* (*http://www.filariasis.us/resources.html*) should then be used to randomly generate numbers that will correspond to the schools/EAs in the list to be selected for surveying.

- For systematic sampling, all schools/EAs on the list will be selected
- For cluster-sample surveys, a minimum of 30 schools/EAs will be selected

Randomized schoolchild/household selection

The *Survey sample builder* tool will calculate a sampling fraction, which is the proportion of children to be surveyed per school (for school surveys) or households to be surveyed per EA (for community surveys). The *Survey sample builder* tool will also calculate the sampling interval (inverse of the sampling fraction) and a random starting point within the sampling interval in order to generate two numbered lists (A and B) to facilitate the selection of schoolchildren and households. After deciding on the order in which schoolchildren or households will be selected in each school or EA, the survey teams randomly select List A or List B. The same lists are used throughout the survey.

If the random starting point on a list is 2.2 and the sampling interval is 2.5, the first child/house selected would be #3, immediately followed by #5 (2.2+ [1x2.5]), #8 (2.2+ [2x2.5]), #10 (2.2+ [3x2.5]), and #13 (2.2+ [4x2.5]). Note that all selections are rounded up to the nearest integer but each calculation itself uses all decimal spots. If the sampling interval equals 1, all children/households in the selected schools/communities will be surveyed and numbered lists will not be required.

The starting number in List B is equal to the sampling interval minus the starting number in List A. Therefore, the use of both lists contributes to sample-size control, since the starting number used at schools or in EAs will not be consistently high or low within the sampling interval.

Absentees

To account for absentees in selected schools/households or refusal to participate, the *Survey sample builder* tool will allow the user to input an expected absentee rate. This rate will vary by country, demography of the EU, and the timing of the survey. For school surveys, programme managers are advised to consult with teachers and the Ministry of Education in advance of the survey to estimate the expected absentee rate excluding children not enrolled. It is recommended to implement the survey during times when absenteeism is projected to be lowest, i.e. at the beginning of the term. If the absentee rate is not known, it might be helpful to visit a few schools to estimate it.

Using the expected absentee rate, the *Survey sample builder* tool will automatically add additional clusters (schools or EAs) and recalculate the sampling interval if required. All selected clusters and individuals from this original selection should be sampled regardless if the target sample size has been met.

Sample size adjustments

If mid-survey and it is apparent that the target sample size will not be reached with the chosen clusters, additional clusters may be randomly selected using only the pool of remaining clusters after the original selection. The additional clusters may also be selected in advance of the survey but only used if necessary.

It is important to survey the additional clusters only after the original clusters are completed and one-by-one until the target sample size has been met. Not all additional clusters chosen need to be sampled if the target has been met; however, in this case, the additional clusters must be surveyed in their order of random selection.

If the target sample size is not met after the survey is complete and it is not feasible to sample additional clusters, a new critical cut-off point can be used in place. This is done by consulting Tables 1 and 2 in the *Manual for survey planners* (reproduced in simpler format here as *Tables A.5.1* and *A.5.2*) and by selecting the row line for the actual sample size and the new corresponding critical cut-off value.

Selecting sites and individuals for inclusion in survey

In countries where both *W. bancrofti* and *Brugia spp*. parasites (e.g. Indonesia) are endemic and the EU can be divided as such, ICTs should be used in the *W. bancrofti* area and Brugia Rapid™ tests in the *Brugia spp.* area. The areas would then be treated as separate EUs with surveys conducted in each.

In overlap areas that are not easily distinguished and divided geographically between *W. bancrofti* and *Brugia spp*., both ICT and Brugia Rapid™ tests will be needed for testing the entire survey population. The survey design and sample size would remain the same with the only exception that each child receives each of the two tests. The number of ICT and Brugia Rapid™ positives will be evaluated separately (i.e. not aggregated together) against the critical cut-off point.

Table A.5.1Sampling intervals, sample sizes and critical values for Transmission Assessment and Post-MDA Surveillance Surveys in *Anopheles* or *Culex* areas

Population surveyed[1,2]	Sampling interval sample	Systematic sampling size (n)	Systematic sampling critical cut-off (d)	Sample size for cluster design[3] (n_cluster)	Number of clusters if cluster-sample survey is		Cluster design critical cut-off (d_cluster)
					school-based	a household survey	
<400	1.0 (census)	N	First integer <0.02N[4]	NA	NA	NA	NA
400	1.4	284	3	*Cluster-sampling not recommended. Use systematic sampling and the corresponding values of n and d*			
600	1.6	365	4				
800	1.8	438	5				
1000	1.9	506	6	759	*Divide the sample size for cluster design by the average number of target-year children per school and round up to the nearest integer. If this integer is <30, then the number of clusters is 30.*	*Divide sample size for cluster design by the estimated average number of target-age children per EA and round up to the nearest integer. If this integer is <30, then the number of clusters is 30.*	9
1200	2.3	520	6	780			9
1400	2.6	530	6	795			9
1600	2.6	594	7	891			11
2000	3.3	606	7	909			11
2400	3.9	614	7	1228			14
2800	4.1	678	8	1356			16
3200	4.6	684	8	1368			16
3600	5.2	688	8	1376			16
4000	5.8	690	8	1380			16
5000	7.1	696	8	1392			16
6000	7.8	762	9	1524			18
8000	10.4	766	9	1532			18
10 000	12.9	770	9	1540			18
14 000	18.0	774	9	1548			18
18 000	23.2	776	9	1552			18
24 000	30.8	778	9	1556			18
30 000	38.5	778	9	1556			18
40 000	47.5	842	10	1684			20
50 000	59.3	842	10	1684			20
≥50 000	Calculate[5]	846	10	1692			20

[1] Refers to whatever population is being surveyed, for example first and second year primary-school children or children aged 6–7 years old in the community.

[2] For a population size between two adjacent Ns in the table, the sampling fraction and d or d_cluster for the lower N should be used.

[3] For the cluster design, the assumed design effects are 1.5 if the population size <2400, and 2.0 if the population size is ≥2400.

[4] For example, there are a total of 300 first- and second-year primary-school children in an EU. All are tested and six are antigenaemic. The EU would fail the TAS because the proportion of children tested who are antigenaemic is 2.0%, not <2.0%. In this case, 0.02 x N = 0.02 x 300 = 6. d (the first integer <6) = 5.

[5] Divide the size of the surveyed population by 846, rounding down to the nearest tenth. For example, if the size of the survey population is 70 000, then the sampling interval is 70 000/846=82.74, rounded down to 82.7.

Table A.5.2 Sampling intervals, sample sizes and critical values for Transmission Assessment and Post-MDA Surveillance Surveys in *Aedes* areas

Population surveyed[1,2]	Sampling interval sample	Systematic sampling size (n)	Systematic sampling critical cut-off (d)	Sample size for cluster design[3] (n_cluster)	Number of clusters if cluster-sample survey is		Cluster design critical cut-off (d_cluster)
					school-based	a household survey	
<1000	1.0	N	First integer <0.01N[4]	NA	NA	NA	NA
1000	1.4	704	4	*Cluster-sampling not recommended. Use systematic sampling and the corresponding values of n and d*			
1200	1.6	730	4				
1400	1.6	854	5				
1600	1.8	876	5		*Divide the sample size for cluster design by the average number of target-year children per school and round up to the nearest integer. If this integer is <30, then the number of clusters is 30.*	*Divide sample size for cluster design by the estimated average number of target-age children per EA and round up to the nearest integer. If this integer is <30, then the number of clusters is 30.*	
1800	2.0	896	5	1344			8
2000	1.9	1014	6	1521			9
2400	2.3	1042	6	1563			9
2800	2.3	1172	7	1758			11
3200	2.6	1188	7	1782			11
4000	3.2	1214	7	1821			11
5000	3.7	1350	8	2700			16
6000	4.4	1364	8	2728			16
7000	5.0	1376	8	2752			16
8000	5.7	1384	8	2768			16
9000	5.9	1510	9	3020			18
10 000	6.6	1516	9	3032			18
12 000	7.8	1524	9	3048			18
14 000	9.1	1530	9	3060			18
16 000	10.4	1536	9	3072			18
≥18 000	Calculate[5]	1540	9	3080			18

[1] Refers to whatever population is being surveyed, for example first- and second-year primary-school children or children 6-7 years old in the community.

[2] For a population size between two adjacent Ns in the table, the sampling fraction and d or d_cluster for the lower N should be used.

[3] For the cluster design, the assumed design effects are 1.5 if the population size <5000, and 2.0 if the population size is ≥5000.

[4] For example, there are a total of 800 first- and second-year primary-school children in an EU. All are tested and 8 are antigenaemic. The EU would fail the TAS because the proportion who are antigenaemic is 1.0%, not <1.0%. In this case 0.01 x N = 0.01 x 800 = 8. d (the first integer <8 = 7.

[5] Divide the size of the surveyed population by 1540, rounding down to the nearest tenth. For example, if the size of the survey population is 20 000, then the sampling interval is 20 000/1540=12.99, rounded down to 12.9.

Personnel

Each survey field team should consist of at least three members: one being responsible for registering children and managing supplies, one phlebotomist and test preparer, and one test reader. A minimum of three to four field teams are recommended but will depend on the size of the EU and number of clusters to cover.

Additionally, if the survey data is being collected electronically, one member from each team should be responsible for collecting and charging the equipment each day. One individual should also be selected among the entire group (i.e. not per each team) to be the 'systems administrator' whose responsibilities are to synchronize and distribute the data that is collected from each field team.

It is very important for programme managers to organize field teams and designate and define roles in advance of the actual field work. A multi-day training session covering the survey design, blood sample procedures, and diagnostic test reading is recommended. Bench aids for conducting ICT or Brugia Rapid™ tests are available for distribution and should be included with the survey preparation materials.

Specimen collection and testing

The following guidelines can be generally used to organize schools and communities for collecting demographic information, blood specimens, and conducting the diagnostic tests. Each country programme, however, should decide on the most appropriate method based on the practical reality of their local setting without disrupting the statistical integrity of the survey design. The chosen method should be employed similarly for all clusters in the EU.

School-based surveys

i. The field team will arrive at a designated school. Upon arrival the team should work with teachers/headmasters/school officials to gather all the first- and second-year primary-school children; if not all such children will be surveyed (i.e. sampling interval >1.0), they should be arranged in a sequence in which they can be counted.

   - The team should also keep a record of the total number of first- and second-year primary-school children attending and absent from each school on the day of the survey. These numbers should be compared to the expected enrolled number and predetermined absentee rate in order to assess if additional clusters may be needed as the survey progresses.

ii. The team leader will flip a coin to decide if List A or List B will be used.

iii. Children are selected according to the numbers on the chosen List. Selection of children should continue until the next number on the List is higher than the total number of first- and second-year primary-school children at the school.

iv. The team should proceed to collect demographic data and blood specimens from the selected children. For school surveys, ICT and Brugia Rapid™ tests can be conducted and read in the field with capillary tubes or micropipettors. If readings are done in the evening or at night, an adequate light source is essential for an accurate result.

v. All positive ICT and Brugia Rapid™ cases should be treated. If desired, programme managers may also choose to do follow-up microfilaraemia testing at night time during the hours of peak microfilaraemia circulation; at this time, status of residence will be checked to detect any significant migration in the area that could affect the impact of MDA rounds; a non-resident could be defined as someone living in the area less than one year.

vi. Repeat steps for each chosen school and additional schools if needed to satisfy the target sample size.

vii. Even if the number of positives exceeds the critical cut-off point, the survey team should continue to collect information on everyone in the sample.

Community-based (household) surveys

i. At each selected EA (community), team leaders should work with village officials/community health workers to verify the number of estimated households in the EA and draw out a walking route that will take them by every single household. Pre-existing sketch maps of the EA may be acquired from the census department and will be useful in this regard. Sensitization of the community should be done well in advance of the actual sample collection date.

ii. The team will then walk the chosen route while enumerating each household. Using the list selected by a coin toss (either A or B), they will sample all 6–7 year olds in each household that has been selected for the survey. If there are no 6–7 year old children in the selected house, the team should proceed to the next house numbered on the list. Selection and sampling will continue until the next number on the list is higher than the total number of households in the EA.

   a. The team should also keep a record of absent children from each household at the time of collection. All efforts should be made to follow-up with these absentees at a later time but within a reasonable schedule to complete the survey. The remaining number of absentees and total number of children surveyed per EA should be recorded and compared to the predetermined absentee rate and expected 6-7 year old population size in order to assess if additional clusters may be needed as the survey progresses.

   b. A designated "mapping team" may be used to enumerate and mark the selected households ahead of the field team.

   c. Alternatively, instead of going house to house, village leaders may be able to prepare ahead of time a list of 6–7 year olds in the EA and arrange for them to gather in a central location at a given time. From the group of all 6–7 year olds, the field team would select the children for sampling according to the numbered lists, similar to the process used for school surveys.

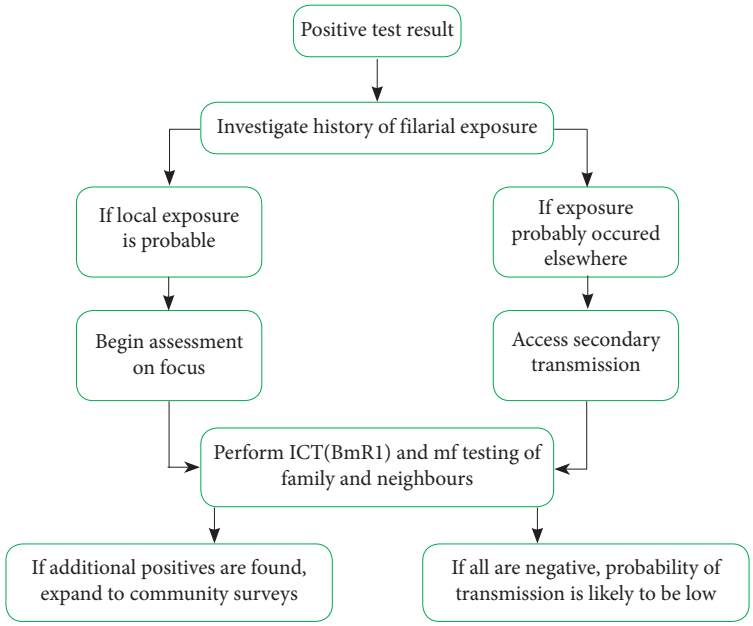
iii. The team should proceed to collect demographic data and blood specimens from all the 6–7 year old children in each selected household. For community surveys, it is recommended to collect the blood samples in EDTA tubes first before doing the ICT or Brugia Rapid™ tests later in a lab setting or other controlled environment. This strategy is found to reduce wait time between sample collections when moving house to house, while also lowering the chance of card reader error.

iv. All positive ICT and Brugia Rapid™ cases should be treated. If desired, programme managers may also choose to do follow-up microfilaraemia testing at night time during the hours of peak microfilaraemia circulation; at this time, status of residence will be checked to detect any significant migration in the area that could affect the impact of MDA rounds; a non-resident could be defined as someone living in the area less than one year.

v. Repeat steps for each chosen EA and additional EAs if needed to satisfy the target sample size.

vi. Even if the number of positives exceeds the critical cut-off point, the survey team should continue to collect information on everyone in the sample.

Algorithm for following up positive ICT or Brugia Rapid™ results in TAS



Data management

All demographic, sample, test, and result data will be collected and recorded using an appropriate database management system.

Data analysis

Critical cut-off values will be used to determine if the level of infection has been reduced to such a level that transmission is likely not sustainable. If a census has been used to conduct the survey, overall prevalence of antigenaemia (antibody for *Brugia spp*. areas) will be calculated to guide the transmission assessment. Additional spatial analyses or multi-site comparison studies may also be performed to enrich survey outcomes.

Programme managers are encouraged to conduct follow up surveys of microfilariae prevalence in communities of antigen-(antibody-) positive children if resources are adequate. This will provide additional information regarding the residual transmission potential.

Effective monitoring, epidemiological assessment and evaluation are necessary to achieve the aim of interrupting LF transmission. This manual is designed to ensure that national elimination programmes have available the best information on methodologies and procedures for (i) monitoring MDA, (ii) appropriately assessing when infection has been reduced to levels where transmission is likely no longer sustainable, (iii) implementing adequate surveillance after MDA has ceased to determine whether recrudescence has occurred, and (iv) preparing for verification of the absence of transmission.

The first edition of this document was published in 2005. In 2010, the STAG-NTD recommended that WHO revise the 2005 document to provide clearer and more feasible methodologies to national programmes on monitoring, epidemiological assessment and evaluation in order to achieve the global target of eliminating LF by 2020. This revised document reflects better understanding of epidemiological aspects of the disease, further field experience, and operational research in monitoring and evaluation of activities to eliminate LF.

Preventive Chemotherapy and Transmission Control (PCT)
Department of Control of Neglected Tropical Diseases (NTD)
World Health Organization
20, Avenue Appia
1211 Geneva 27, Switzerland

http://www.who.int/neglected_diseases/en

9 789241 501484